Deliverable 3.1 (WP3)

Initial Ontologies for Toxicity Data

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Purpose of Document:	The OpenTox Deliverable Report WP3 – D3.1 on initial ontologies introduces a controlled vocabulary, identifies relevant toxicological endpoints, lists the most promising data sources and discusses the selection of appropriate data storage and exchange formats

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Summary

In recent times the word and concept of ontology has been adopted from its original philosophical domain by the information sciences. In computer and information science, an ontology is a formal representation of a set of concepts within a domain, and the relationships between those concepts. With this connotation, ontology is a word widely used in many biological research areas as well. Within this practical perspective the construction of a biological ontology consists of: a) selection of entities or objects to be included; b) definition of a controlled vocabulary; c) recognition of hierarchies, when existing.

The definition of ontology and controlled vocabulary is very useful to standardize and organize the chemical toxicological database for the OpenTox project. Its construction will consist of two main steps: first, the selection of the toxicological endpoints to be included; second, the definition of the type and extent of information for each endpoint.

The selection of the toxicological endpoints will focus on those endpoints recognized internationally as critical for the testing of chemicals. The main sources of information are: a) the OECD guidelines for testing of chemicals[1] and b) the toxicological endpoints relevant to the assessment of chemicals in the EU[2]. The main source of data for the OpenTox database will be the public domain which can be categorized into:

- textual databases (e.g., IARC[3], NTP[4]);
- machine readable files (e.g., .sdf) that can be immediately used by the modellers for the (Q)SAR analyses in the OpenTox platform (e.g., DSSTox[5], ISSCAN[6], AMBIT[7], ITEM-REPDOSE[8]);
- large and quite complex databases on the Internet (e.g., PubChem[9], ACToR[10]).

Because of the varying data quality level of the various databases, higher priority would be given to databases directly curated by project's participants.

A wide spectrum of (Q)SAR approaches, as applied to toxicity, exist today, ranging from coarse-grain to fine-tuned ones. However, all the various (Q)SAR modelling approaches share the need of a highly structured information as starting point. Based on a careful research, two publicly available schemas appear to fulfil the above criteria: the OECD harmonized templates[11] and the ToxML (Toxicology XML standard) schema[12]

It appears that the OECD harmonized templates have the advantage of being closer to the schemas established by the regulators for the industry to submit their data. However, this schema is quite generic, and does not lend easily itself to the needs of the OpenTox project in terms of scientific databases and scientific computing.

[1] http://www.oecd.org/department/0,3355,en_2649_34377_1_1_1_1_1,00.html accessed on Feb 17th 2010
[2] http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.htm#B accessed on Feb 17th 2010
[3] http://www.iarc.fr/en/websites/index.php accessed on Feb 17th 2010
[4] http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm accessed on Feb 17th 2010
[5] http://www.epa.gov/ncct/dsstox/index.html accessed on Feb 17th 2010
[6] http://www.iss.it/ampp/dati/cont.php?id=233&lang=1&tipo=7 accessed on Feb 17th 2010
[7] http://ambit.sourceforge.net/ accessed on Feb 17th 2010
[8] http://publica.fraunhofer.de/starweb/servlet.starweb?path=pub0.web&search=N-49776 accessed on Feb 17th 2010
[9] http://pubchem.ncbi.nlm.nih.gov/ accessed on Feb 17th 2010
[10] http://actor.epa.gov/actor/ accessed on Feb 17th 2010
[11] http://www.oecd.org/document/13/0,3343,en_2649_34365_36206733_1_1_1_1,00.html accessed on Feb 17th 2010
[12] http://www.leadscope.com/toxml.php accessed on Feb 17th 2010

On the other hand, the ToxML schema has all the features necessary for accommodating large amounts of data at different levels of complexity, and for creating hierarchies within ontology constructs. However, a preliminary analysis aimed at mapping the content of selected databases onto the two schemas has shown that in either case some adaptation and modification is necessary.

Thus, it was decided to expand the mapping exercise to further databases: this will point out strengths and weaknesses of the schemas, and to necessary improvements.

1. General definition of ontology and its role in information science and biology

Ontology (from the Greek ὠν, genitive ὀντος: of being <part. of εἶναι: to be> and -λογία: science, study, theory) in philosophy is the study of the nature of being, existence or reality in general, as well as of the basic categories of being and their relations. Traditionally listed as a part of the major branch of philosophy known as metaphysics, ontology deals with questions concerning what entities exist or can be said to exist, and how such entities can be grouped, related within a hierarchy, and subdivided according to similarities and differences[13].

1.1 Ontology in information science

From its original philosophical domain, the word and concept of ontology has been adopted by the information sciences. An ontology in computer science and information science is a formal representation of a set of concepts within a domain, and the relationships between those concepts. It is used to reason about the properties of that domain, and may be used to define the domain. Thus, an ontology is a "formal, explicit specification of a shared conceptualisation". An ontology provides a shared, or controlled vocabulary, which can be used to model a domain – i.e., the type of objects and/or concepts that exist, and their properties and relations. The controlled vocabulary is a collection of preferred terms that are used to assist in more precise retrieval of content. Controlled vocabulary terms can be used for categorizing content, building labelling systems, and creating style guides and database schema. One type of a controlled vocabulary is a taxonomy. Ontologies are used in artificial intelligence, the Semantic Web, software engineering, biomedical informatics, library science, and information architecture as a form of knowledge representation about the world or some part of it[14]. The Ontology-based informatics approaches provide very powerful tools to organize and retrieve information (McGuinness 2003)[15].

1.2 Application of ontologies in biology

In biology, the explosion of the amount of data generated through high-throughput techniques has lead to the need of organizing these data in a logical way; to this purpose, the concept of ontology has been adopted.

1.2.1 Gene Ontology (GO) project as one of the most successful examples of systematic description of biology

The most successful example of systematic description of biology is the Gene Ontology (GO) project. GO is widely used in biological databases, annotation projects and computational analyses for annotating newly sequenced genomes, text mining, network modelling and clinical applications, among others. GO has two components: the ontologies themselves, which are the defined terms and the structured relationships between them (GO ontology); and the associations between gene products and the terms (GO annotations). GO provides both ontologies and annotations for three distinct areas of cell biology: molecular function, biological process, and cellular component or location (Rhee et al 2008). A GO annotation associates a gene with terms in the ontologies and is generated either by a curator or automatically through predictive methods. Genes are associated with as many terms as appropriate as well as with the most specific terms available to reflect what is

[13] http://en.wikipedia.org/wiki/Ontology accessed on Feb 17th 2010

[14] http://en.wikipedia.org/wiki/Ontology_(information_science) accessed on Feb 17th 2009

[15] http://www.ksl.stanford.edu/people/dlm/papers/ontologies-come-of-age-mit-press-(with-citation).htm accessed on Feb 17th 2010

currently known about a gene. When a gene is annotated to a term, associations between the gene and the terms' parents are implicitly inferred. Because GO annotations to a term inherit all the properties of the ancestors of those terms, every path from any term back to its root(s) must be biologically accurate or the ontology must be revised. For example, if a gene is known to be specifically involved in 'vesicle fusion', it will be annotated directly to that term, and it is implicitly annotated (indirectly) to all of its parents' terms, including 'membrane fusion', 'membrane organization and biogenesis', 'vesicle-mediated transport', 'transport' and so on, back to the root node. Thus, a gene annotated to vesicle fusion can be retrieved not only with this term, but also with all of its parent terms, increasing flexibility and power when searching for and making inferences about genes.

1.2.2 Practical aspects of biological ontologies

The above discussion points to the need for a high level of accuracy of the data and underlying theory which are organized into an ontological representation. Thus "man-made" fields, like e-commerce, web-search engines, libraries catalogues, etc, where almost all the details of the underlying information can be defined with a high level of accuracy, can be translated into sophisticated ontologies that include: controlled vocabularies, glossary, thesauri, together with explicit hierarchy, frames and value restrictions.

On the contrary, fields like biology have a much looser underlying theory; as a consequence, biological ontologies are relatively simpler. As a matter of fact, the adoption of ontologies in molecular and systems biology originated not only from the practical need to organize and retrieve information, but also from the idea that organizing and clustering genes, proteins, RNAs, etc… at various levels (from coarse to very fine), could get to a deeper understanding of biology. However, recent scientific advancements have changed many previous beliefs; for example, the central dogma according to which one gene gives rise to one protein has been shaken by the recognition that completely different proteins, with completely different functions, can be originated from the same stretch of DNA or RNA. Because of the present fluidity of the biological theory, biological ontologies have lost much of their ultimate philosophical scope, and have mainly retained the more practical aspects referring to information science. Within this perspective, most often the construction of a biological ontology consists of: a) the selection of entities or objects to be included; b) the definition of a controlled vocabulary; and c) the recognition of hierarchies, when existing.

2. Toxicological endpoints for the OpenTox database

The definition of ontology and controlled vocabulary is extremely important to the construction of the database for the OpenTox project. It will contribute to the necessary standardization and rational organization of data, thus facilitating both vertical (e.g., within one toxicological endpoint) and horizontal (e.g., through different endpoints) retrievals.

It will consist of two main steps: first, the selection of the toxicological endpoints to be included; second, the definition of the type and extent of information for each endpoint, and their internal relationships and hierarchies.

2.1 OECD endpoints to be included in OpenTox database

The OpenTox database on toxicity will include the toxicological end points for which data are required under the REACH regulation. In current toxicological testing, these endpoints are addressed by both *in vitro* and animal experiments carried out according to OECD guidelines.

The toxicological endpoints considered by REACH are the following (Lilienblum et al 2008):

- Skin irritation, skin corrosion;
- Eye irritation;

- Dermal sensitisation;
- Mutagenicity;
- Acute oral toxicity;
- Acute inhalative toxicity;
- Acute dermal toxicity;
- Repeated dose toxicity (28 days);
- Repeated dose toxicity (90 days);
- Reproductive toxicity screening;
- Developmental toxicity;
- Two-generation reproductive toxicity study;
- Toxicokinetics;
- Carcinogenicity study.

The OECD guidelines for testing of chemicals[16] are published on the Internet. Whereas there is no official list of OECD endpoints (test guidelines are developed according to the needs of member countries), and no official OECD approach to toxicity testing, interesting background information on criteria for toxicity testing has been developed as SIDS (Screening Information Data Set). The information of the SIDS and which guidelines can be used to fill them can be found in Chapter 2 of the Manual for Investigation of High Production Volume (HPV) Chemicals[17].

Additional information on the testing methods and strategies is available in the Test Methods Regulation[18]:and at the European Chemicals Agency's web site[19].

3. Data sources for the OpenTox database

The main source of data for the OpenTox database will be the public domain. At present, the toxicity data in the public domain are spread in many and varied sources and databases. They can be categorized into:

- Textual databases (e.g., IARC[20], NTP[21]);

- Machine readable files (e.g., .sdf) that include both structures and data, and that can be immediately used by the modelers for the (Q)SAR analyses in the OpenTox platform (e.g., DSSTox[22], ISSCAN[23], AMBIT[24], ITEM-REPDOSE[25]);

[16] http://www.oecd.org/document/40/0,3343,en_2649_34377_37051368_1_1_1_1,00.html accessed on Feb 17th 2010
[17] http://www.oecd.org/document/7/0,3343,en_2649_34379_1947463_1_1_1_1,00.html accessed on Feb 17th 2010
[18] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:142:0001:0739:EN:PDF accessed on Feb 17th 2010
[19] http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.htm#B accessed on Feb 17th 2010
[20] http://www.iarc.fr/en/websites/index.php accessed on Feb 17th 2010
[21] http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm accessed on Feb 17th 2010
[22] http://www.epa.gov/ncct/dsstox/index.html accessed on Feb 17th 2010
[23] http://www.iss.it/ampp/dati/cont.php?id=233&lang=1&tipo=7 accessed on Feb 17th 2010
[24] http://ambit.sourceforge.net/ accessed on Feb 17th 2010
[25] http://publica.fraunhofer.de/starweb/servlet.starweb?path=pub0.web&search=N-49776 accessed on Feb 17th 2010

- Large and quite complex databases on the Internet (e.g., PubChem[26], ACToR[27]). Here there is no direct access to the underlying file(s). Portions of the information (with structures and data) can be downloaded, however the use of non-trivial informatics scripts is required.

The above differences in the types of data sources are entwined with differences in the quality of data (some databases may contain contradictory results, with no critical selection), and with changes with time (updates). Because of such difficulties, priority in the selection of databases for OpenTox will be given to databases directly curated by project's participants.

As part of the OpenTox effort in WP3, a carefully curated list of candidate databases has been contributed by ITEM (see Review of Data Sources including formats and REACH relevance).

3.1 Databases that will be used in the first phase of the OpenTox project

For a first phase, the databases proposed as directly curated by the OpenTox participants are:

ITEM:
- repeated doses (fields to be decided)

ISS:
- (rodent) carcinogenicity (Yes/no response (overall, and in the four experimental groups: rat, mouse, male, female); Carcinogenic Potency TD50);
- Ames test Mutagenicity (Yes/no response (overall, and in the different bacterial strains));
- in vivo micronucleus in rodents (Yes/no response, species, sex, route).

3.2 Databases that will be included in OpenTox in the second phase of the project

In a second phase, additional databases will be included in OpenTox. Among others, the databases in DSSTox will have a priority. These are in the form of machine-readable files (.sdf), cover several toxicological endpoints, and the quality of chemical identification has been revised by Ann Richard's group at the US EPA, whereas the responsibility for the quality of the biological calls relies on the authors of the individual databases. Overall the quality of the DSSTox databases is high; however there may be specific cases where contradictions with other databases should be resolved.

A main repository of public data is PubChem. It gives access to, and re-uses existing resources such as the cluster of toxicological databases TOXNET[28]. PubChem is going to incorporate the ToxCast[29] project data as well. In spite of the fact that the quality of data is -obviously- not homogeneous, PubChem will continue to play a central role in the field. However, PubChem does not consist of separate files that can be easily downloaded; downloading data simultaneously for a set of molecules requires quite sophisticated informatics scripts. A procedure that permits an user-friendly access to portions of PubChem data would be highly desirable. The possibility of integrating such a procedure in OpenTox's framework is currently being studied in WP1 and WP2.

4. OpenTox controlled vocabulary and hierarchy

The OpenTox database on toxicological data is essentially meant to be used as support for developing (Q)SAR models within the OpenTox platform. Thus, its design is going to take into account the requirements of (Q)SAR modelling.

[26] http://pubchem.ncbi.nlm.nih.gov/ accessed on Feb 17th 2010
[27] http://actor.epa.gov/actor/ accessed on Feb 17th 2010
[28] http://toxnet.nlm.nih.gov/ accessed on Feb 17th 2010
[29] http://www.epa.gov/ncct/toxcast/ accessed on Feb 17th 2010

4.1 Different (Q)SAR modelling approaches: the need for a highly structured information as starting point

A wide spectrum of (Q)SAR approaches, as applied to toxicity, exist today, ranging from coarse-grain to fine-tuned ones. Broad classes are (Benigni and Bossa 2008):

- structure alerts, which are substructures and reactive groups linked to the induction of chemical toxicity (e.g., carcinogenicity). They are used for preliminary hazard characterization, are quite popular with regulators and industry, and most often are based on, and provide to the users mechanistic information;

- QSARs for noncongeneric sets of chemicals (e.g., Lazar, PASS), which generate probabilities of being active / inactive (and to what extent) for compounds with very different structures;

- QSARs for congeneric sets of chemicals (e.g., Hansch approach), which use mechanistically-based descriptors, and describe how relatively small changes in structure can provoke variations in activity. Series of very similar (highly congeneric) chemicals are usually developed by industries.

Despite their differences, all the various (Q)SAR modelling approaches share the need of a highly structured information as starting point. This includes the selection of ontologies, with controlled vocabulary and hierarchies.

A precious background material has been provided by IBMC (Sergey Novikov and Natalya Skvortsova), consisting of detailed description of toxicity terms arranged in alphabetical order (see Controlled Vocabulary).

4.2 Schemas for the OpenTox Ontology

A thorough search performed within WP3 has pointed to two publicly available schemas fulfilling the above criteria: the OECD harmonized templates[30], and the ToxML (Toxicology XML standard) schema[31].

4.3 The OECD harmonized templates

The OECD harmonized templates correspond to the IUCLID5 XML schemas, which are meant to be used by industry when submitting the documentation on their chemicals to EU authorities. For each endpoint, the OECD harmonized templates define series of fields: the example (***Figure 1***) is from Template 72, Carcinogenicity.

Thus, since they are generic enough to be able to include data on endpoints with different characteristics, in principle the OECD harmonized templates provide a substantial basis for building an ontology. However, they are not very formalized and they leave much space to free text entering.

```
ADMINISTRATIVE DATA

    DATA SOURCE

        reference, author, title, report date, data protection, etc.

MATERIALS AND METHODS

        test guideline, deviations from guideline, etc.

    Test materials
```

[30] http://www.oecd.org/document/13/0,3343,en_2649_34365_36206733_1_1_1_1,00.html accessed on Feb 17th 2010

[31] http://www.leadscope.com/toxml.php accessed on Feb 17th 2010

```
        test material, identifier (CAS RN), details, ....

    Test animals

        Species, strain, sex, ...

    Administration exposure

            Route of administration, , type of inhalation exposure, vehicle,
....

    Examination

        observations, examinations, pathology, statistics, etc.

RESULTS AND DISCUSSION

        endpoint, effect levels, effect type, etc.

    Observations

OVERALL REMARKS, ATTACHMENTS

    Clinical signs, body weight, etc.
```

Figure 1: Example of field definition by the OECD harmonized templates (Template 72, Carcinogenicity)

4.4 ToxML (Toxicology XML standard) schema

ToxML is a public initiative led by scientists at Leadscope, Inc[32] to promote adoption and use of controlled vocabularies and XML schema for storing chemical toxicity data. The LIST (Leadscope In Silico Toxicology) Focus Group consisted of industry, government and academic clients of Leadscope, and other invited and interested parties. Leadscope has recruited toxicity domain experts for developing relevant controlled vocabularies (initially in the areas of mutagenicity and carcinogenicity, then including genetic toxicity, chronic/subchronic, and reproductive and developmental studies). Public funding of this effort through a NIST Advanced Technology Program Grant ensures that a basic ToxML schema, viewer, and data entry form are being made freely available to promote public adoption of the standardized format and vocabularies. ToxML has the two-fold objective of: a) supporting broadly encompassing and meaningful representations of toxicology experiments, with hierarchical schemes including various levels of complexity; and b) indexing the data with the chemical structures, as to permit the widest range of chemical biological interrogations of the database (Richard et al 2008)[33].

The following (***Figure 2***) is an excerpt from the generic schema of ToxML, applicable for all toxicity studies.

```
ToxicityStudies

    AllStudyTypes

        Study
```

[32] http://www.leadscope.com/ accessed on Feb 17th 2010

[33] http://www.epa.gov/ncct/dsstox/CoordinatingPublicEfforts.html accessed on feb 17th 2010

```
            Background
            ...
            Tests
                Test
                    NegativeTestControls
                        ...
                    PositiveTestControls
                        ...
                    TestCondition
                        ...
                    TestResults
                    ...
                    TestSystem
                        AnimalCount : InexactValue
                        HostOrganism : String
                        IndicatorOrganism : String
                        InitialAge : String
                        InitialWeight : String
                        MembraneSize : String
                        MembraneStorageConditions : String
                        MembraneThickness : String
                        MembraneType : String
                        MetabolicActivation : String
                        PercentS9 : String
                        S9Type : String
                        Sex : Sex
                        Species : String
                        Strain : String
                        StrainCharacteristics : String
```

```
                    Supplier : String
                    TargetCell : String
                    TestSystemComments : String
                Treatments
                    TreatmentGroup
                        ...
                        DosageRegimen
                        ...
                        Results
                            AbsorptionPenetrationData
                            ...
                            IndividualResults
                            ResultFindings
                        ......
```

Figure 2: Generic schema of ToxML applicable for all toxicity studies

5. Results and Conclusions

A very fruitful discussion on the merits and limitations of the two above mentioned schemas has taken place among the OpenTox partners. A number of analyses have been performed as well, in particular by IDEA. The ISSCAN carcinogenicity database has been fully mapped to ToxML's XSD schema and partially to the OECD-Harmonized Templates schema (see ISSCAN <-> ToxML mapping and ISSCAN data in ToxML format as illustrations of this work). In principle, both schemas can be used, and both have pros and cons.

ToxML seems to be closer to the needs of building databases aimed at scientific computing (but adaptations and extensions are necessary).

OECD-HT seems to be more suitable for textual archives than for scientific computing. Its main advantage is that it contains schemas for all the various endpoints of regulatory relevance, and there is a rich documentation (Schematron, etc.). In addition, OECD-HT is already adopted by the important IUCLID5 regulatory database at EChA. Adaptations and extensions seem to be necessary also here. However our first impressions are that due to the volume and level of complexity of OECD-HT much more time and efforts would be required to adapt it to the needs of the OpenTox database.

Thus, a conclusion is that more detailed mapping is required in order to decide which schema to adopt. It has been decided to continue the mapping exercise with further databases, e.g., those for aquatic toxicity (EPAFHM[34] in DSSTox), repeated doses toxicity (ITEM-REPDOSE), endocrine disruptors (NCTRER[35] in DSSTox), and a second carcinogenicity database (CPDBAS[36] in DSSTox).

6. References

Benigni R, Bossa C (2008), Predictivity and reliability of QSAR models: the case of mutagens and carcinogens., Toxicol.Mechanisms Meth. 18: 137-147

Lilienblum W, Dekant W, Foth H, Gebel T, Hengstler JG, Kahl R, Kramer PJ, Schweinfurth H, Wollin KM (2008), Alternative methods to safety studies in experimental animals: role in the risk assessment of chemicals under the new European Chemicals Legislation (REACH), Regulat.Toxicol. 82: 211-236

McGuinness DL (2003), Ontologies come of age., in Spinning the semantic web: bringing the World Wide Web to its full potential., ed. Fensel D, Hendler J, Lieberman H, and Wahlster W, MIT Press, Boston

Rhee SY, Wood V, Dolinski K, Draghici S (2008), Use and misuse of gene ontology annotations., Nat.Revs.Genetics 9: 509-515

Richard AM, Yang C, Judson RS (2008), Toxicity Data Informatics: Supporting a New Paradigm for Toxicity Prediction., Toxicol.Mechanisms Meth. 18: 103-11

[34] http://www.epa.gov/ncct/dsstox/sdf_epafhm.html accessed on Feb 17th 2010
[35] http://www.epa.gov/ncct/dsstox/sdf_nctrer.html accessed on Feb 17th 2010
[36] http://www.epa.gov/NCCT/dsstox/sdf_cpdbas.html accessed on Feb 17th 2010

ISSCAN <-> ToxML mapping

ISSCAN_v3a_1153_19Sept08.1222179139 <---> ToxML-v24.05.2006 Mapping (revision 2009021201)					
Data Source		http://www.iss.it/binary/ampp/cont/ISSCAN_v3a_1153_19Sept08.1222179139.sdf			
XML Schema		http://www.leadscope.com/toxml/downloads/toxml_public.xsd.zip			
№	ISSCAN	ToxML		Comments	
		Full Path	Value	1	2
1	MOL Structure ID	/Compounds/Compound/Structure/Molfile/Header/Line1	*var*	OK	
2	MOL Connection Table	/Compounds/Compound/Structure/Molfile/ConnectionTable	*var*	OK	
3	Substance ID	/Compounds/Compound/OtherIds/Id@type="SubstanceID"	*var*	OK	
4	ChemName	/Compounds/Compound/Names/Name@type="chemName"	*var*	OK	
5	Synonyms	/Compounds/Compound/Names/Name@type="synonym"	*var*	OK	
6	CAS	/Compounds/Compound/Ids/Id@type="cas"	*var*	OK	
7	Reference	/Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Background/References/Reference	*var*	OK	
8	MolWeight	/Compounds/Compound/Datasets/Datum/Name /Compounds/Compound/Datasets/Datum/Value	MolWeight *var*	OK OK	
9	Formula	/Compounds/Compound/Structure/MolecularFormula/Value	*var*	OK	
10	SMILES	/Compounds/Compound/OtherIds/Id@type="smiles"	*var*	OK	
11	TD50_Rat	/Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestSystem/Species /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Type /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Value/Value /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Value/Units	Rat TD50 *var* *var* OR unitless	OK OK OK OK	
12	TD50_Mouse	/Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestSystem/Species /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Type /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Value/Value /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Value/Units	Mouse TD50 *var* *var* OR unitless	OK OK OK OK	
13	Canc	/Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Type /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Value/Value /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Value/Units	Canc *var* unitless	OK OK OK	
14	SAL	/Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Type /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Value/Value /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Value/Units	SAL *var* unitless	OK OK OK	
15	Rat_Male_Canc	/Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestSystem/Species /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestSystem/Sex /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Type /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Value/Value /Compounds/Compound/ToxicityStudies/ChronicStudies/Study/Tests/Test/TestResults/EndPoints/EndPoint/Value/Units	Rat Male Canc *var* unitless	OK OK OK OK OK	
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Legend:

var	variable (value read from file)
OK	mapping OK, successfully validated against http://www.leadscope.com/toxml/downloads/toxml_public.xsd.zip

ISSCAN data in ToxML format


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Review of Data Sources including formats and REACH relevance

Toxicological endpoints relevant under REACH

The REACH legislative requires that data must be available on intrinsic properties of all substances produced in volumes greater than 1 tonne/year. Annex VII to X describe the testing needs and strategy for chemicals depending on the volume manufactured. Information on intrinsic properties of the substance can also be provided using alternative testing methods if the conditions described in Annex XI are met. Annex XI explicitly states that qualitative and quantitative QSARs can be used instead of experimental data if

- Results are derived from a QSAR model whose scientific validation has been established
- The substances are covered in the applicability domain of the model
- Results are adequate to classification and labelling and/or risk assessment of the chemical
- Adequate and reliable documentation of the QSAR model is available.

However, these general rules have not yet been substantiated by the Commission.

According to this definition QSAR might be possible to replace any of the testing needs required under REACH in Annex VII to X.

Table 1 gives a brief overview on the required test for human health endpoints.

Several publications have been published to evaluate for which kind of tests there will be a need for alternative testings with regard to costs, time and animal welfare. The term alternative tests include *in vitro* methods, grouping of substances and read across (e.g. category approach), QSAR models, as well as weight of evidence approaches or human epidemiological studies.

Van der Jagt K [37] estimated the number of tests needed under REACH. Here the most demanded tests are those relevant for all chemicals from Annex VII to X, indicating that skin sensitization would be a relevant endpoint for alternative testing strategies. However, in terms of costs and animal welfare the more complex toxicological endpoints like chronic toxicity or reprotoxicity gain importance. Here, long and therefore cost intensive studies have to be conducted which will need many animals (Figure 4).

Also Pedersen et al. [38] concluded that in total most studies will be performed for the endpoints skin sensitization, eye irritation and *in vivo* mutagenicity (in decreasing order). However, the most cost intensive tests under REACH will be developmental-, two-generation, *in vivo*-mutagenicity and subchronic toxicity studies.

These considerations may also have influenced the selection of endpoints of the EU project CAESAR (Project no. 022674 – SSPI; http://www.caesar-project.eu/). It develops QSAR models for the REACH legislation and concentrates on five endpoints:

- Bioconcentration factor
- Skin sensitization
- Mutagenicity
- Carcinogenicity
- Developmental reprotoxicity

[37] Van der Jagt K, Munn S, Torslov J, de Bruijn J (2004) Alternative approaches can reduce the use of test animals under Reach. *Report EUR 21405 EN;* http://ecb.jrc.it

[38] Pedersen F, de Bruijn J, Munn S & van Leeuwen K (2003). Assessment of additional testing needs under REACH. Effects of QSARs, risk based testing and voluntary industry initiatives. EUR 20863 EN

Table 1: Testing needs described in ANNEX VII to X for human health endpoints

	Annex VII **>1t/a**	**Annex VIII** **>10t/a** **(additional)**	**Annex IX** **>100 t/a** **(additional)**	**Annex X** **>1000 t/a** **(additional)**
required endpoint	Skin/Eye irritation (in vitro) Skin Sensitization (in vivo) Mutagenicity (in vitro, Ames) Acute Toxicity (oral)	Skin/Eye irritation (in vivo) Mutagenicity (mammalian cells/cytogenicity) Acute Toxicity (inhalation/dermal) Subacute Toxicity (28 days) Screening for reprotoxicity (OECD 421/422)	Subchronic Toxicity (90 days) Prenatal developmental tox (OECD 414) Reprotoxicity (2-generation)	Chronic Toxicity (> 12 months) Carcinogenicity (2 years)

*Figure 3: Estimated testing needs under Reach [**Error! Bookmark not defined.**]*

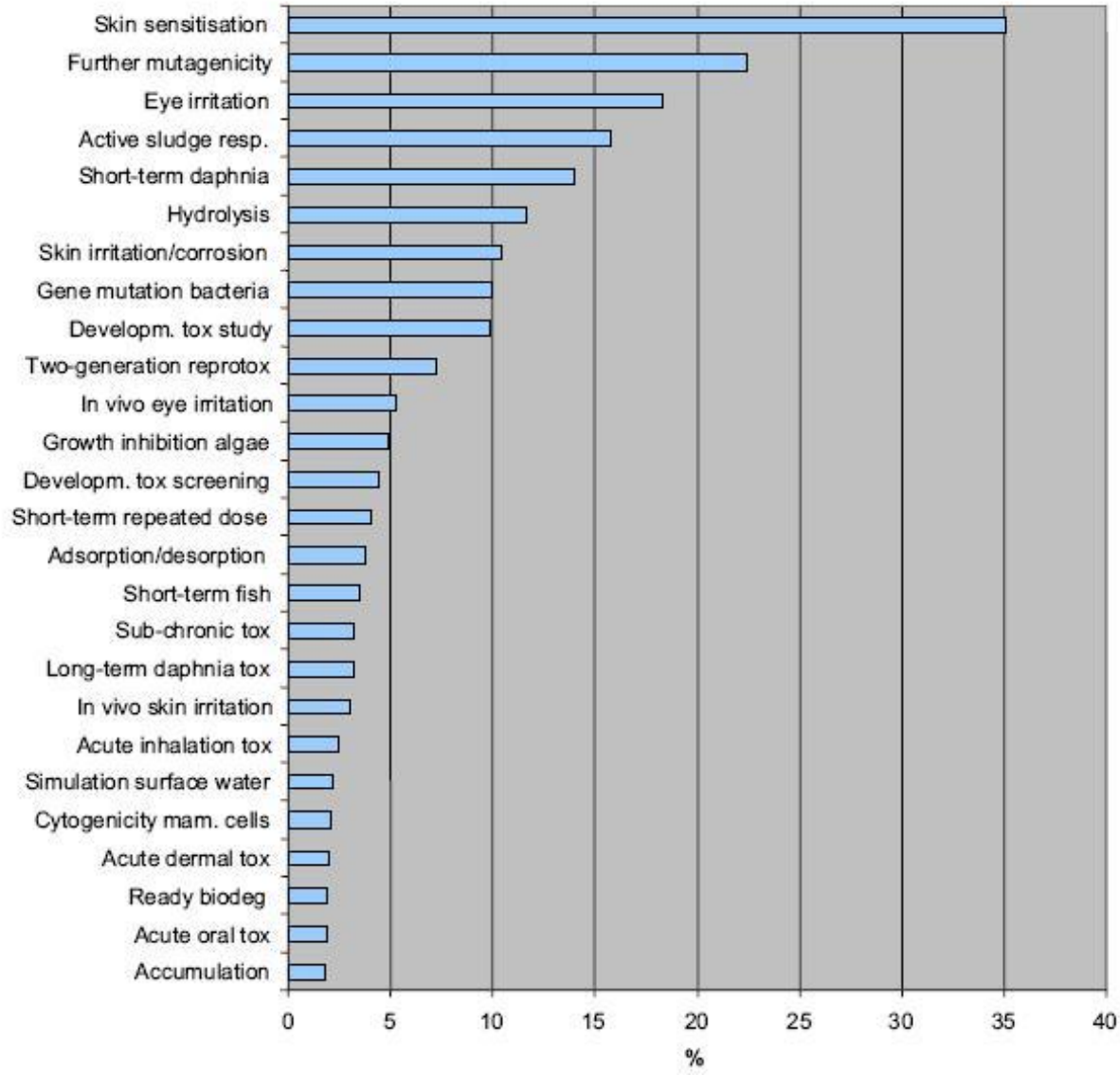

*Figure 4: One example of an estimation of most cost-intensive tests needed under REACH. [**Error! Bookmark not defined.**]*

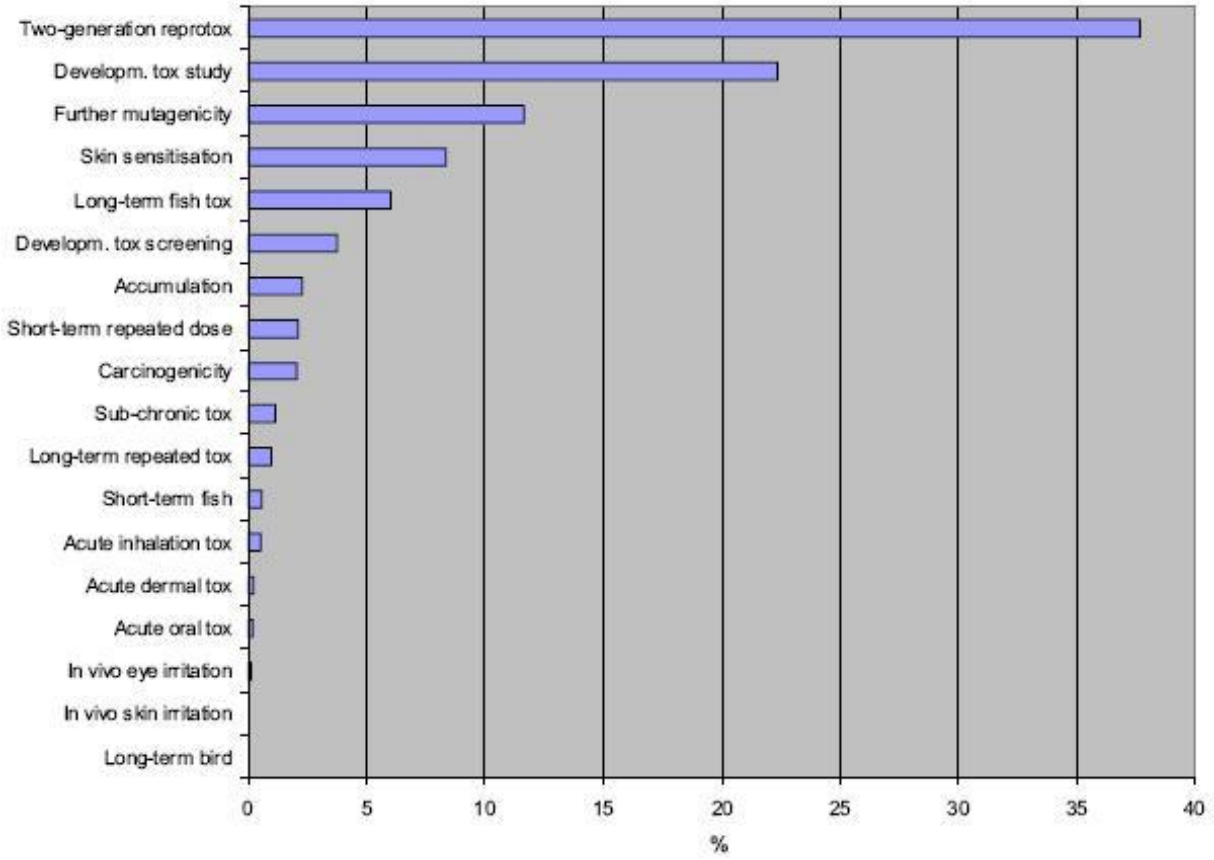

*Figure 5: Second example of an estimation of most cost-intensive tests needed under REACH [**Error! Bookmark not defined.**].*

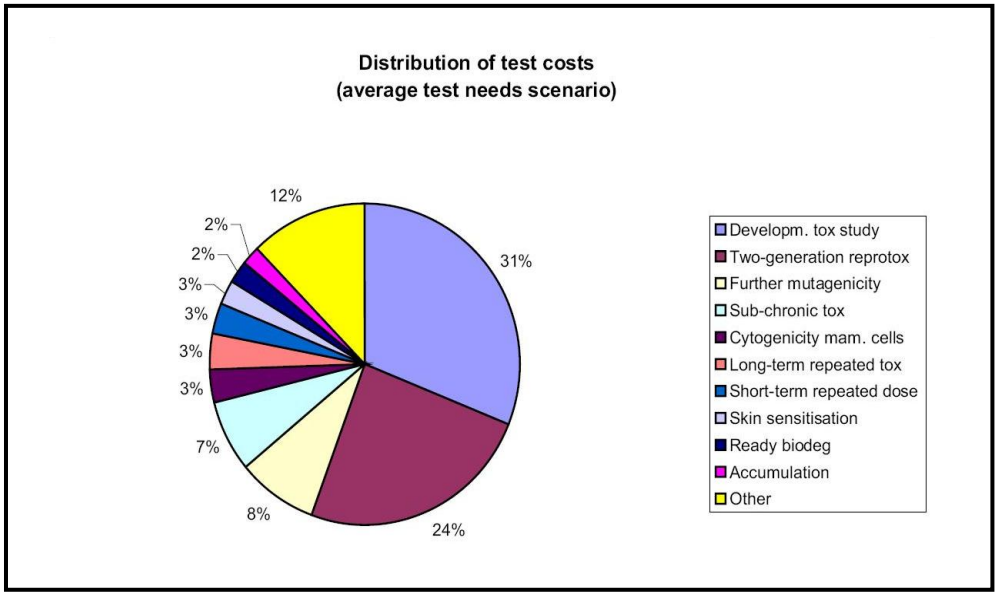

Table 2: Data sources for relevant endpoints under REACH

Endpoint	Name of database	Source	Format	Comment
Reproductive/developmental Tox	ILSI – Developmental Toxicity SAR database	http://www.ilsi.org/		under development
	PubChem Bioassay	http://pubchem.ncbi.nlm.nih.gov/	multiple	
	Leadscope /FDA databases	Leadscope		not public
	FDA TERIS Dataset	CAESAR EU Project		Terato-genicity
	DART	TOXNET http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?DARTETIC	mulitple	
Reproductive Tox (Two-generation studies)	FeDTex	FhG-ITEM 100 compounds	ACCESS	
Mutagenicity	DSSTox (CPDBAS) Carcinogenic Potency Database Summary Salmonella Mutagenicity	http://www.epa.gov/NCCT/dsstox/sdf_cpdbas.html	Sd.file	
	PubChem Bioassay	http://pubchem.ncbi.nlm.nih.gov	multiple	
	Leadscope FDA SAR Genetox Database	http://www.leadscope.com/toxicity_databases		not public
	Gene-Tox-Genetic Tox Data Bank			
Skin sensitization	Several databases	CAESAR EU Project		
Sub- to chronic toxicity	RepDose	FhG ITEM	ACCESS	

	Munro database	Publication [39]	Exel/pdf	
Carcinogenicity	ISSCAN	http://www.iss.it/ampp/dati/cont.php?id=233&lang=1&tipo=7	Sd.file	
	CCRIS-chemical Carcinogenesis Research Information System	TOXNET http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CCRIS	multiple	
Several endpoints	OSIRIS database	Collection of databases on toxicoglogical endpoints relevant for REACH	multiple	under development – publicly available when published
	DB-ALM Alternative in vitro tests for several endpoints	http://ecvam-dbalm.jrc.ec.europa.eu/	pdf	Tests for: skin/eye irritation; nephro-toxicity, embryo-toxicity, terato-genicity

The EU-project OSIRIS (http://www.osiris-reach.eu/) develops integrated testing strategies (ITS) to reduce animal testing needs under REACH. For this purpose a database on several endpoints has been set up, collecting available toxicological data from various sources. The OSIRIS database as well as the ITS tool will be publicly available latest at the end of the project (in 2011). The overview of available data in the OSIRIS database depicted in Table 3 has been kindly provided by Mark Hewitt from the group of Mark Cronin in Liverpool (Liverpool John Moores University, School of Pharmacy and Chemistry).

[39] Munro IC Ford RA, Kennepohl E and Sprenger JG (1996) Correlation of a structural class with no-observed-effect-levels: a proposal for establishing a treshold of concern. Food and Chemcial Toxicology **34**, 829-867.

Table 3: Overview about the content of the OSIRIS database, kindly provided by Mark Hewitt from the group of Mark Cronin (Liverpool John Moores University, School of Pharmacy and Chemistry). References are at the end of the table.

General				
Database	**Assay/ Species/ Time**	**Chemicals (no. and type)**	**Source**	**Comments**
ChemIDPlus	Multiple species	382'146 entries	ChemIDPlus website (http://chem.sis.nlm.nih.gov/chemidplus/)	All accessible toxicity data is accompanied with original references
Cronin et al. (2002)	Mouse LD50	Pyridine and 20 hydroxy, alkyl, pyridyl and N-oxide derivatives	Ref. [1]	
ESIS	Multiple Species		European chemical Substances Information System (http://ecb.jrc.ec.europa.eu/esis/)	ESIS can be used to obtain data relating to multiple species and endpoints, including:
Combines data from:				
EINECS		100'204 chemicals	European INventory of Existing Commercial chemical Substances	Acute oral, inhalation and dermal toxicity
ELINCS		4'381 chemicals	European List of Notified Chemical Substances	Corrosiveness and irritation
NLP		703 chemicals	No-Longer Polymers	Sensitisation
BPD		210 chemicals	Biocidal Products Directive	Repeated dose toxicity
PBT or vPvB		127 chemicals	Persistent, Bioaccumulative, and Toxic (PBT); very Persistent and very Bioaccumulative (vPvB)	Genetic toxicity in vivo and in vitro
C&L			Classification and Labelling	Carcinogenicity
HPVCs and LPVCs		HPVC – 2'782 chemicals; LPVC – 7'829 chemicals	High Production Volume Chemicals (HPVCs); Low Production Volume Chemicals (LPVCs)	Reproductive toxicity
IUCLID		2'604 chemicals	International Uniform ChemicaL Information Database	Developmental toxicity / teratogenicity
ORATS		141 chemicals	Online EUropean Risk Assessment Tracking System	

Haws et al. (2006)	Relative Potency Estimates (REPs), mouse	Numerous dixion or dioxin-like compounds	Ref. [2]	
HSDB	Various species	Approxiamtely 5'000 chemcials	Hazardous Substances Data Bank (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?hsdbb.htm)	Can be searched using compound name, CAS number, etc.; Results can be downloaded.
IMAGETOX Project Dataset	Rat (LD50 in mg/kg)	235 pesticides	Data were sourced from: RTECS	Contains rat LD50 data, compound name and CAS numbers.
Lessigiarska et al (2007)	Multiple (human, rat, mouse)	27 chemicals / drugs	Ref. [3], with original data obtained from Ref. [4]	
Llewellyn (2007)	Potencies in mouse (µmol)	30 saxitoxins	Ref. [5]	
Mumtaz et al (1995)	LOAELs in rats	234 chemically and structurally diverse compounds	Ref. [6]	
NCCOS	Multiple (rat, mouse, rabbit)	Currently 349 Pharmaceuticals	NCCOS - Pharmaceuticals in the Environment, Information for Assessing Risk (http://www.chbr.noaa.gov/peiar)	Compilation of measured and predicted values. Data can be searched and exported as .xsl or .cvs file.
PubChem Database	Multiple species	Numerous	PubChem Website	Can be searched via compound name, structure or bio-assay, Links to many other data sources (DSSTox, ChemIDPlus, etc.)
MEIC and NICEATM	Oral LD50 for rat and mouse (plus average human dose)	50 chemicals	Multicenter Evaluation of In Vitro Cytotoxicity (MEIC); NTP (National Toxicology Program) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)	

Travis and White (1988)	Maximum Tolerated Dose (MTD) for multiple species	27 chemicals	Ref. [7]	

Carcinogenicity				
Database	**Assay/ Species/ Time**	**Chemicals (no. and type)**	**Source**	**Comments**
Wang and Bai (1998)	Rat and mouse oral LD50	95 alcohols	Ref. [8]	LD50 data are given in the publication. Compounds were placed into four categories based on LD50 data.
CAESAR Project Carcinogenicity Dataset	Stated as active (specified rat TD50) or inactive	806 compounds	CAESAR EU Project. Originally sources from the CPDB carcinogenicity potency database. The CAESAR database has been quality checked.	SDF file also included Dataset is effectively a subset if the DSSTox (CPDB) dataset
CPDB	Multiple species	1'548 chemicals	Carcinogenicity Potency DataBase (http://potency.berkeley.edu/cpdb.html)	Two different datasets (NCI/NTP dataset and literature main dataset).
CCRIS	Multiple (mouse, rat)	Over 8'000 chemicals	Chemical Carcinogenesis Research Information System (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CCRIS)	Database can be searched online via TOXNET. Results can then be downloaded.
ISSCAN Database	Rat/mouse	1'153 chemicals	http://www.iss.it/ampp/dati/cont.php?id=233&lang=1&tipo=7	Freely available in .xls form
Y. Koleva Carcinogenicity Dataset	Rat/mouse	251 chemicals	Data taken from Ref. [9] (English translation of original 1998 German publication.)	Rat / mouse toxicities are given in mg/kg and mmol/kg in .xls form
PubChem Bioassay	Multiple assays	Multiple datasets	http://pubchem.ncbi.nlm.nih.gov/	Contains EPA DSSTox database.
DSSTox (DBPCAN)	Classification	80 active compounds	DSSTox EPA Water Disinfection By-Products with Carcinogenicity Estimates	

DSSTox (CPDBAS)	Rat TD50	577 active compounds	DSSTox Carcinogenic Potency Database Summary Rat Bioassay Results	
DSSTox (CPDBAS)	Classification	582 active compounds	DSSTox Carcinogenic Potency Database Summary MultiCellCall Results	
DSSTox (CPDBAS)	Mouse TD50	445 active compounds	DSSTox Carcinogenic Potency Database Summary Mouse Bioassay Results	
DSSTox (CPDBAS)	Hamster TD50	44 active compounds	DSSTox Carcinogenic Potency Database Summary Hamster Bioassay Results	
DSSTox (CPDBAS)	Dog / primate TD50	15 active compounds	DSSTox Carcinogenic Potency Database Summary Dog and Primates Bioassay Results	
DSSTox (CPDBAS)	Classification	806 compounds	DSSTox Carcinogenic Potency Database Summary SingleCellCall Results	
Kazius, J.	Ames test – mutagenicity	4'337 – various compounds	Ref. [10]	Classifications – mutagen / non-mutagens CAESAR EU Project

Mutagenicity				
Database	**Assay/ Species/ Time**	**Chemicals (no. and type)**	**Source**	**Comments**
Leadscope FDA SAR Genetox Database	Multiple – Including mammalian and in vitro	8'412 compounds	LeadScope (http://www.leadscope.com/fda_databases/)	Available for purchase. License need to be obtained
PubChem Bioassay	Multiple assays	Multiple datasets	http://pubchem.ncbi.nlm.nih.gov/	Contains EPA DSSTox database.
DSSTox (CPDBAS)	Classification	395 active compounds	DSSTox Carcinogenic Potency Database Summary Salmonella Mutagenicity	

Skin Sensitisation				
Database	Assay/ Species/ Time	Chemicals (no. and type)	Source	Comments
Cronin and Basketter dataset	Guinea pig maximisation test	259 – various chemicals	Ref. [11]	Two datasets have been combined into a single dataset CAESAR EU Project
Gerberick dataset	LLNA, mouse	210 – various chemicals	Ref. [12]	
Schlede dataset	Rat, mouse, human	244 – various chemicals	Ref. [13]	
Patlewicz et al. dataset	LLNA, mouse	44 – various chemicals	Ref. [14]	

Endocrine Disruption				
Database	Assay/ Species/ Time	Chemicals (no. and type)	Source	Comments
Androgen Receptor Binding Dataset	LogRBA	202 compounds	Ref. [15]	
DSSTox (NCTRER)	ER RBA / classification	232 compounds (131 active)	DSSTox National Center for Toxicological Research Estrogen Receptor Binding Database	
EASYRING	Various (various RBAs, EC50, PC50)	2101 compounds (many with no data)	Endocrine Disruption Database – FULL	EASYRING EU Project
EASYRING	Various (various RBAs, EC50, PC50)	514 compounds (all with some data)	Endocrine Disruption Database – EDITED	
EC	List of ED classifications at expert meeting	146 compounds	http://ec.europa.eu/environment/docum/pdf/bkh_annex_13.pdf	List freely available.

Estrogen Receptor Binding Dataset	LogRBA	232 compounds	Ref. [16], Ref. [17]	
FDA	Various species and assays	3257 entries	FDA Endocrine Disruptor Knowledge Base (EDKB)	Freely available JAVA tool containing a large database.

Reproductive / Developmental Toxicity				
Database	**Assay/ Species/ Time**	**Chemicals (no. and type)**	**Source**	**Comments**
PubChem Bioassay	Multiple assays	Multiple datasets	http://pubchem.ncbi.nlm.nih.gov/	Contains EPA DSSTox database.
Enslein et al. Terato-genesis Database	Terato-genic potential (0 to 1)	670 compounds	Ref. [18]	Screening criteria are given in the paper along with all raw data.
Gombar et al. Terato-genicity Database I	Rat	374 compounds	Ref. [19]	TOPKAT developmental toxicity database was used as a starting point.
Gombar et al. Terato-genicity Database II	Classifi-cation (+/-)	171 compounds	Ref. [20], with data orignially sourced from Ref. [18]	A series of local QSAR models were developed based upon chemical class. Data for all compounds is given in the article.
Jelovsek et al. (1989)	Rabbit, Rat, Mouse, Hamster and Human Data	157 compounds	Ref. [21]	Hosted on the ECB website.The data is available as .SDF, .MOL or in .xls format
ILSI	Rat	under development	ILSI (International Life Sciences Institute) - Developmental Toxicity Database for Improving SAR Models, (http://www.ilsi.org)	Not yet released publically

LeadScope / FDA Databases:				
FDA CFSAN 2008 Repro-Developmental Database	Multiple, including rats and rabbits.	312 food ingredients	FDA Centre for Food Safety and Applied Nutrition (CFSAN). Available for purchase through the Leadscope website	Available for purchase.
FDA CDER) 2008 Repro-Developmental Database	Multiple, including rats and rabbits.	58 drug compounds	Centre for Drug Evaluation and Research (CDER). Available for purchase through the Leadscope website	Available for purchase.
Placental Mambrane Transfer Datasets	Human Placental Perfusion		Ref. [22]	QSAR models have been developed from each dataset for placental transfer.These models are given and dicussed. ReProTect – EU Project
Dataset 1		78 diverse compounds		
Dataset 2		56 diverse compounds		
Dataset 3		21 diverse compounds		
Dataset 4		11 Antiviral compounds		
Dataset 5		8 Tocolytic compounds		
Sussman et al. (FDA TERIS Dataset)		293 – various chemicals	Ref. [23]	Teratogencicity – binary data CAESAR EU Project
Gombar et al Terato-genicity database	Rat	374 compounds	Ref. [19]	TOPKAT developmental toxicity database was used as a starting point.

Chronic Toxicity				
Database	Assay/ Species/ Time	Chemicals (no. and type)	Source	Comments
RepDOSE	Rat, mouse, dog	650 compounds	Repeated Dose Database (RepDOSE); www.fraunhofer-repdose.de	

Other data				
Database	Assay/ Species/ Time	Chemicals (no. and type)	Source	Comments
Data from Russian Primary literature	Multiple species		Search for data on individual endpoints	
Sens-it-iv EU Project Database	Multiple species		http://www.sens-it-iv.eu/	The project will result in the development of an inductive database, ultimately with a web-interface. However, this is still in development
EDETOX EU Project Database	Percutaneous penetration - Multiple species, including humans		http://www.ncl.ac.uk/edetox/theedetoxdatabase.html	The database can be viewed online or down-loaded in MS Access form. EDETOX EU Project
Silastic membrane flux (logJ) Dataset	Polydimethylsiloxane membrane	256 compounds	Ref. [24]	

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Controlled Vocabulary

Term	Definition	Ref.
Abatement	The reduction in degree or intensity of pollution [13]	80
Abiotic degradation or transformation	Degradation of a chemical (f.e.pesticide) via purely physical or chemical mechanisms. Examples include hydrolysis and photolysis.	36
Absorbed dose	The amount of a substance penetrating the exchange boundaries of an organism after contact. Absorbed dose for the inhalation and ingestion routes of exposure is calculated from the intake and the absorption efficiency. Absorbed dose for dermal contact depends on the surface area.	165
Absorption	Absorption is the passage of one substance into or through another. [5]. 1. The penetration of one substance into or through another. 2. Specifically, the penetration of a substance into the body from the skin, lungs, or digestive tract. [13]	80, 165
Absorption barrier	Any exposure surface that may allow diffusion of an agent into a target. Examples of absorption barriers are the skin, lung tissue, and gastrointestinal tract wall (cf. exposure surface).	50
Acceptable daily intake (ADI)	An estimate of the daily exposure dose that is likely to be without deleterious effect even if continued exposure occurs over a lifetime [8] . The amount of a chemical a person can be exposed to on a daily basis over an extended period of time (usually a lifetime) without suffering deleterious effects [1]. Estimated maximum amount of an agent, expressed on a body mass basis, to which an individual in a (sub) population may be exposed daily over its lifetime without appreciable health risk. Related terms: *Reference Dose, Tolerable Daily Intake [26].* *M*aximum amount of a substance to which a subject may be exposed daily over the subject's lifetime without appreciable health risk. [11]	21, 55, 77, 125
Acceptable range of oral intake (AROI).	The AROI is designed to limit deficient and excess intakes in healthy populations and is set for different age–sex groups and physiological states such as pregnancy and lactation. To facilitate comparisons, AROIs are discussed in relation to other risk assessment approaches. Trace elements currently regarded by the World Health Organization as essential for human health are iron (WHO, 1988), zinc, copper, chromium, iodine, cobalt, molybdenum and selenium.	124
Acceptable risk	This is a risk management term. The acceptability of the risk depends on scientific data, social, economic, and political factors, and on the perceived benefits arising from exposure to an agent [26]. type of risk such that the benefits derived by an organism, a	21, 55

	population, or an ecological system outweigh the adverse effects that might affect them as a result of being administered or exposed to a particular agent [11]. Risk level judged to be compatible with the protection of animal, plant, and public health, taking into account epidemiological, biological, social and economical factors. It is a management decision with regard to the permissibility of a hazard, a decision made (in the risk management process) about the safety of a regulatory decision or the acceptability of a hazardous event (SPS Agreement).	
Accident	1. That occurrence in a sequence of events which usually produces unintended injury, death or property damage.[13]	80
Accident type	1. Describes the occurrence leading to injury or property damage.	80
Accuracy	The degree to which a measurement reflects the true quantitative value of a variable [5] 1. The degree of agreement between a measured value and the true value; usually expressed as +/- percent of full scale.[13]. Closeness of agreement between the result of a measurement and the (conventional) true value of the measure and. Note 1. Use of the term precision for accuracy should be avoided. Note 2. True value is an ideal concept and, in general, cannot be known exactly [112].	14, 80, 165
Act of God	An act occasioned by an unanticipated grave natural disaster.	80
Action level	Regulatory levels recommended by EPA for enforcement by Food and Drug Administration and United States Department of Agriculture when pesticide residues occur in food or feed commodities for reasons other than the direct application of the pesticide. As opposed to "tolerances" which are established for residues occurring as a direct result of proper usage, action levels are set for inadvertent residues resulting from previous legal use or accidental contamination. In the Superfund program, the existence of a contaminant concentration in the environment high enough to warrant action or trigger a response under SARA and the National Oil and Hazardous Substances Contingency Plan. The term is also used in other regulatory programs [8]. For food commodities, an administrative maximum residue ***Limit*** (MRL) used by regulatory authorities to initiate action where no legally defined **MIU** has been established. 2. For the environment, concentration of a pesticide in air, **soil** or water at which emergency measures or preventative actions are to be taken. The concentration of a contaminant which, if exceeded, triggers treatment or other requirements which a water system must follow. It is the level of lead or copper which, if exceeded in over 10% of the homes tested, triggers treatment.	77, 144
Acute	Having a sudden onset or lasting a short time. An acute stimulus is severe enough to induce a response rapidly. The word acute can be used to define either the exposure or the response to an exposure	80, 165

	(effect). The duration of an acute aquatic toxicity test is generally 4 days or less and mortality is the response usually measured.[5]. 1. Acute-diseases or responses with short and generally severe course (often due to high pollutant concentrations).[13]	
Acute (one-hour) inhalation Reference exposure levels (rels)	The acute REL is an exposure that is not likely to cause adverse effects in a human population, including sensitive subgroups, exposed to that concentration for one hour on an intermittent basis (or in the case of reproductive/developmental endpoints several hours as indicated in individual toxicity summaries) . These health based acute RELs are applicable to risk character-ization of air releases. RELs may not protect hypersensitive individuals (those exhibiting idiosyncratic responses that cannot be predicted from studying the health effects of the substance). OEHHA recommends that these acute RELs be used to evaluate exposures that occur no more frequently than every two weeks in a given year. The two-week interval was chosen because in most acute toxicology experiments two weeks is the duration of time an animal is observed for signs of adverse outcome following exposure. An assumption in making this recommendation is that the REL is protective of adverse health effects that are not cumulative; thus, the effects of each peak exposure are inde-pendent of previous or subsequent peak exposures that occur as often as every two weeks. This recommendation is only valid for substances that do not bioaccumulate. When bioaccumulation is known to occur and body burden is associated with an adverse effect, longer interexposure periods should be specified.	76
Acute exposure	Exposure by the oral, dermal, or inhalation route for 24 hours or less [1] A contact between an agent and a target occurring over a short time, generally less than a day [49].	50, 125
Acute hazard or toxicity	Acute toxicity is assessed using observations of accidental human exposures or by conducting LD50 tests on experimental animals, usually rodents.	
Acute reference concentration (arfc)/fcute reference dose (ARFD)	An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for an acute duration (24 hours or less) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments	125
Acute toxicity	Any poisonous effect produced within a short period of time following exposure, usually up to 24-96 hours, resulting in biological harm and often death [8]. 1. Any poisonous effect produced within a short period of time following exposure, usually up to 24-96 hours, resulting in biological harm and often	77, 80, 125

	death.[13] Any poisonous effect produced within a short period of time following an exposure, usually 24 to 96 hours. [1].	
Adaptive effect	An adaptive effect enhances an organism's performance as a whole and/or its ability to withstand a challenge. An example of an adaptive effect is an increase in hepatic smooth endoplasmic reticulum, but only if hepatic metabolism reduces the chemical's toxicity.	12
Added (additional) risk (AR)	The difference between the cancer incidence under the exposure condition and the background incidence in the absence of exposure [8]. The calculated difference in risk of a particular condition between those who are exposed and those who are not. This measure is derived by subtracting the rate (usually incidence or mortality) of the disease among the unexposed persons (Pu) from the corresponding rate among the exposed (Pe), i.e., AR= Pe-Pu. The AR is an absolute measure of the excess risk attributed to exposure.	47, 77, 125
Additivity	Defining the usefulness of data for hazard/risk assessment purposes. When there is more than one study, the greatest weight is attached to the study that is the most reliable and relevant (“key” studies). When the "effect" of a combination of chemicals is estimated by the sum of the exposure levels or the effects of the individual chemicals [42]. When the "effect" of the combination is estimated by the sum of the exposure levels or the effects of the individual chemicals. The terms "effect" and "sum" must be explicitly defined. Effect may refer to the measured response or the incidence of adversely affected animals. The sum may be a weighted sum (see "dose addition") or a conditional sum (see "response addition") [109].	118, 131
Administered dose	The mass of a substance given to an organism and in contact with an exchange boundary (i.e., gastrointestinal tract) per unit wet body weight (BW) per unit time (e.g., mg/kgBW/day).	78, 165
Adsorption	Adsorption is the adhesion of molecules of gas, liquid, or dissolved solids to a surface. The term also refers to a method of treating wastes in which activated carbon is used to remove organic compounds from wastewater.	165
Advanced air emission control devices	Air pollution control equipment, such as electrostatic precipitators and high energy scrubbers, that are used to treat an air discharge which has been treated initially by equipment including knockout chambers and low energy scrubbers.[13]	80
Advection	Process of transport of an atmospheric property, or substance within the atmosphere, solely by the mass motion of the atmosphere.	80
Adverse ecological effects	Changes that are considered undesirable because they alter valued structural or functional characteristics of ecosystems or their components. An evaluation of adversity may consider the type,	124, 165

	intensity, and scale of the effect as well as the potential for recovery [5,. 40].	
Adverse effect	A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge[1]. Any biochemical change, functional impairment, or pathologic lesion which impairs performance and reduces the ability of an organism to respond to additional challenge. An adverse effect may have different degrees of severity, and should be distinguished from adaptive (beneficial) effects and compensatory (neutral) effects.[14]. Change in the morphology, physiology, growth, development, reproduction or life span of an organism, system, or (sub) population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress, or an increase in susceptibility to other influences [26]. change in morphology, physiology, growth, development, or life span of an organism, which results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress, or an increase in susceptibility to other environmental influences[11]	21, 27, 55, 125
Aerodynamic diameter	Expression of aerodynamic behavior of an irregularly shaped particle in terms of the diameter of an idealized particle; that is, aerodynamic diameter is the diameter of a sphere of unit density that has aerodynamic behavior identical to that of the particle in question. Thus, particles having the same aerodynamic diameter may have different dimensions and shapes [13]. The diameter of a sphere with unit density that has aerodynamic behavior identical to that of the particle in question; an expression of aerodynamic behavior of an irregularly shaped particle in terms of the diameter of an idealized particle. Particles having the same aerodynamic diameter may have different dimensions and shapes [1]	80, 125
Aerodinamic particle size	Sphere of unit density that has aerodynamic behavior identical to that of the particle in question.	80
Aerosol	System in which the dispersion medium is a gas and the dispersed phase (composed of solid particles or liquid droplet) does not settle out under the influence of gravity.[13]. A suspension of liquid or solid particles in air [1].	80, 125
Aerosol particles	Solid particles <10−6 m in diameter, dispersed in gas.	80
Aesthetic effect	Offensive to the senses.	99
Age-standardized rate	An age-standardized rate is a weighted average of the age-specific rates, where the weights are the proportions of a standard	12

	population in the corresponding age groups (q.v.). The potential confounding effect of age is removed when comparing age-standardized rates computed using the same standard population.	
Age weights	Factor specifying the relative value of a year of healthy life lived at different ages. The DALY can incorporate non-uniform age weights which give less weight to years of life lived in early childhood and at older ages.	12
Agent	Any physical, chemical, or biological entity that can induce an adverse response (synonymous with stressor). [5]. Any physical, chemical, or biological entity that can induce an adverse response (synonymous with stressor) [40]. A chemical, biological, or physical entity that contacts a target [49].	50, 124, 165
Aggregate dose:	The amount of a single substance available for interaction with metabolic processes or biologically significant receptors from multiple routes of exposure.	118
Aggregate exposure	including all anticipated dietary exposures for which there is reliable information." Aggregate exposure will typically include exposures from food, drinking water, residential uses of a pesticide, and other nonoccupational sources of exposure. The amount of a chemical available at the biological exchange boundaries (e.g., respiratory tract, gastrointestinal tract, skin) for all routes of exposure. A process for developing an estimate of the extent of a defined population to a given chemical by all relevant routes and from all relevant sources.	118
Aggregate risk	The risk associated with all pathways & routes of exposure to a single chemical.	118, 149
Air emissions	The release or discharge of a pollutant (from a stationary source) into the ambient air. For anthropogenic sources this may involve release (1) by means of a stack or (2) as a fugitive dust, mist or vapor as a result inherent to the manufacturing or formulating process. Pollutants may also be discharged from mobile sources, from area sources such as roads and fields, and from non-manufacturing, stationary sources.	80
Air monitoring	The continuous sampling for, and measuring of, pollutants present in the atmosphere.	80
Air pollutant	Dust, fumes, mist, smoke and other particulate matter, vapor, gas, odorous substances, or any combination thereof; any air pollution agent or combination of such agents, including any physical, chemical, biological, radioactive (including source material, special nuclear material, and by-product material) substance or matter which is emitted into or otherwise enters the ambient air.	80
Air pollution	The presence in the outdoor atmosphere of any dust, fumes, mist,	80

	smoke, other particulate matter, vapor, gas, odorous substances, or a combination thereof, in sufficient quantities and of such characteristics and duration as to be, or likely to be, injurious to health or welfare, animal or plant life, or property, or as to interfere with the enjoyment of life or property	
Air quality criteria	The levels of pollution and lengths of exposure above which adverse effects may occur on health and welfare.	80
Air quality standards	The level of pollutants prescribed by law or regulation that cannot be exceeded during a specified time in a defined area	80
Air sampling	The collection and analysis of air samples for detection or measurement of radioactive substances, particulate matter, or chemical pollutants	80
Airborne particulates	Total suspended particulate matter found in the atmosphere as solid particles or liquid droplets. Chemical composition of particulates varies widely, depending on location and time of year. Airborne particulates include: windblown dust, emissions from industrial processes, smoke from the burning of wood and coal, and motor vehicle or non-road engine exhausts	77
Alara ("as low as reasonably achievable,")	Acronym for means making every reasonable effort to maintain exposures to ionizing radiation as far below the dose limits as practical, consistent with the purpose for which the licensed activity is undertaken, taking into account the state of technology, the economics of improvements in relation to state of technology, the economics of improvements in relation to benefits to the public health and safety, and other societal and socioeconomic considerations, and in relation to utilization of nuclear energy and licensed materials in the public interest. (see 10 CFR 20.1003)	77
Analog(s)	Analog is a generic term used to describe substances that are chemically closely related. Structural analogs are substances that have similar or nearly identical molecular structures. Structural analogs may or may not have similar or identical biological	118
Analysis	Detailed examination of anything complex made in order to understand its nature or to determine its essential features	21
Anecdotal data	Data based on the description of individual cases rather than controlled studies.	125
Antagonism	Interference or inhibition of the effect of one chemical by the action of another [8]. **Antagonism:** The ability of a substance to prevent or interfere with another substance interacting with its biological targets, thereby reducing or preventing its [42]. When the effect of the combination is less than that suggested by the component toxic effects. Antagonism must be defined in the context of the definition of "no interaction," which is usually dose or response addition [109].	77, 118, 131
Applied dose	The amount of a substance in contact with the primary absorption	48

	boundaries of an organism (e.g., skin, lung, gastrointestinal tract) and available for absorption. In exposure assessment, the amount of a substance in contact with the primary absorption boundaries of an organism (e.g., skin, lung tissue, gastrointestinal track) and available for absorption. The amount of a substance presented to an absorption barrier (i.e., skin, lung, or digestive tract) and available for absorption, but not yet having crossed the outer boundary of an organism. The amount of a substance in contact with the primary absorption boundaries of an organism (e.g., skin, lung, gastrointestinal tract) and available for absorption. Applied Amount of chemical in as above **Dermal:** (mg chem/kg soil) (kg soil directly touching skin) (% (e.g., of chem in soil actually skin, lungs, gastrointestinal touching skin) = mg chem. touching skin) = mg chem. actually touching skin. **Respiratory:** lung) = mg chemical actually (µg chem/m air) (m air mcg/m3 directly touching lung) (% of chemical actually touching lung absorption. **Oral:** (mg chem/kg food) (kg food consumed/day) (% of chemical touching g.i. tract) = mg chemical actually touching g.i. tract absorption (also absorbed dose rate: mg/day) chemical available to organ or cell (dose rate: mg chemical available to organ/day)	
Appropriate assessment factor (ASF)	Coefficient used for calculated Concern Concentration (CC). The assessment factors are listed below versus the type of toxicity data available: field chronic no-effect-concentration -ASF 1,0; laboratory chronic no-effect-concentration - ASF 10; laboratory acute toxicity data - ASF 100; single laboratory acute toxicity data - ASF 1000. The CC is calculated by dividing the toxicity value to the most sensitive organism in the environmental compartment by the appropriate ASF. Typically a base set of data for evaluating the potential ecological effects of new chemical would include determining the acute toxicity the chemical to 3 classes of aquatic organisms; fish, invertebrate and algae. Results are expressed as the concentration which results in death, immobilization or lack of growth; respectively during exposure for the stated time period. This test series might include a 96-hr lethal concentration to 50% (LC50) of the fish (rainbow trout), a 48-hr effect concentration to 50% (EC50) of the invertebrates (*Daphnia magna*) exposed and a 96-hr growth inhibition which results in a reduction in growth rate by 50% to an algae (*Selenastrum capricornutum*). Tests which measure end points such as lethality are considered acute tests while tests which measure end points such as reproduction and growth over the full life-cycle of the test organism are considered chronic. If the base set of data, acute toxicity data to 3 species, were provided the CC would be equal to the toxicity measured with respect to most sensitive organism divided by ASF, 100. For example, Solutia was considering manufacturing a new polymer additive which had been found to have acute toxicities greater than	21

	1,000 mg/L to the 3 species tested. Since no chronic toxicity data is available, we would assume that the CC is greater than 10 mg/L.	
Assessment	Evaluation or appraisal of an analysis of facts and the inference of possible consequences concerning a particular object or process [26]. Combination of analysis of facts and inference of possible consequences concerning a particular object [11]	21, 55
Assessment endpoint	Qualitative/Quantitative expression of a specific factor with which a risk may be associated as determined through an appropriate risk assessment [26]. Quantitative expression of a specific factor with which a risk may be associated as determined through an appropriate risk assessment [11]. An explicit expression of the environmental value that is to be protected, operationally defined by an ecological entity and its attributes. For example, salmon are valued ecological entities; reproduction and age class structure are some of their important attributes. Together "salmon reproduction and age class structure" form an assessment endpoint [40].	21, 55, 124
Assessment factor	Numerical adjustment used to extrapolate from experimentally determined (doseresponse) relationships to estimate the agent exposure below which an adverse effect is not likely to occur [26]. Related terms: *Safety Factor, Uncertainty Factor.*	21, 55
Attributable risk	The rate of a disease in exposed individuals that can be attributed to the exposure. This measure is derived by subtracting the rate (usually incidence or mortality) of the disease among nonexposed persons from the corresponding rate among exposed individuals.	77
Autocorrelation	The correlation between adjacent observations in time or space.	48
Average daily dose (ADD)	Dose rate averaged over a pathway-specific period of exposure expressed as a daily dose on a per-unit-body-weight basis. The ADD is usually expressed in terms of mg/kg-day or other mass-time units.	125
Background level (environmental)	In air pollution, the level of pollutants present in ambient air from natural sources. More generally, the level of pollution present in environmental medium attributable to natural or ubiquitous sources [8]. 1. In air pollution, the level of pollutants present in ambient air from natural sources. 2. More generally, the level of pollution present in any environmental medium attributable to natural or ubiquitous sources [13] Two types of background levels may exist for chemical substances: (a) Naturally occurring levels: Ambient concentrations of substances present in the environment, without human influence; (b) Anthropogenic levels: Concentrations of substances present in the environment due to human-made, non-site sources (e.g., automobiles, industries) [1]. The amount of an agent in a medium	48, 77, 80, 125

	(e.g., water, soil) that is not attributed to the source(s) under investigation in an exposure assessment. Can be naturally occurring or anthropogenic. (Note: natural background is the concentration of an agent in a medium that occurs naturally or is not the result of human activities) [49]	
Baseline risk assessment	A baseline risk assessment is an assessment conducted before cleanup activities begin at a site to identify and evaluate the threat to human health and the environment. After remediation has been completed, the information obtained during a baseline risk assessment can be used to determine whether the cleanup levels were reached [5]	165
Basis	The data used by an organization to calculate a risk value. The basis is listed on *ITER*'s noncancer risk value tables. Examples of the basis include: No Observed Adverse Effect Level (NOAEL), No Observed Effect Level (NOEL), Lowest Observed Adverse Effect Level (LOAEL), or Lowest Observed Effect Level (LOEL). This basis is generally divided by a number of uncertainty factors to calculate the risk value (e.g., RfD, TC, MRL).	12
Basis (adj)	This is the NOAEL, LOAEL, or benchmark dose identified in the critical study, adjusted for continuous exposure, that was administered in a laboratory animal experiment, or to which humans were exposed occupationally or in controlled studies. For example, for a gavage study in which the animals were administered the compound 5 days/week, the administered dose would be multiplied by 5/7 to obtain a continuous dose. Similarly, for an inhalation study carried out 6 hours/day, the administered concentration would be adjusted by a factor of 6/24 to obtain a continuous dose.	12
Basis (exp)	This is the NOAEL, LOAEL, or benchmark dose identified in the critical study. It is expressed as the actual dose or concentration that was administered in a laboratory animal experiment, or to which humans were exposed occupationally or in controlled studies. This dose/concentration has not been adjusted for continuous exposure.	12
Benchmark dose (BMD) or concentration (BMC)	A dose or concentration that produces a predetermined change in response rate of an adverse effect (called the benchmark response or BMR) compared to background. (http://permanent.access.gpo.gov/lps38234/cfpub.epa.gov/ncea/cfm/bmds.cfm-ActType=default.htm)	125
Benchmark response (BMR)	An adverse effect, used to define a benchmark dose from which an RfD (or RfC) can be developed. The change in response rate over background of the BMR is usually in the range of 5-10%, which is the limit of responses typically observed in well-conducted animal experiments.	125
Benefit	The degree to which effects are judged desirable. The change in	80

	the baseline value of each decision objective as a result of implementing a decision option. For comparison of benefits across decision objectives, benefits for individual decision objectives will have to be normalized, using a scaling function. Benefits may be unrelated to a change in risk, as in addressing a socioeconomic benefit to a community or in achieving a decision objective in a manner consistent with external preferences. For any given decision objective, benefits may increase (desirable), decrease (undesirable), or remain the same following implementation of a decision option.	
Best available control measures (BACM):	A term used to refer to the most effective measures (according to EPA guidance) for controlling small or dispersed particulates from sources such as roadway dust, soot and ash from woodstoves and open burning of brush, timber, grasslands, or trash [8]	77
Best available (control) technology , best demonstrated available technology (BDAT)	A BDAT is a technology that has demonstrated the ability to reduce a particular contaminant to a lower concentration than other currently available technologies. BDATs can change with time as technologies evolve[5]. An emission limitation (including a visible emission standard) based on the maximum degree of reduction for each pollutant subject to regulation under the [Clean Air] act which would be emitted from any proposed major stationary source or major modification which the Administrator, on a case-by-case basis, taking into account energy, environmental, and economic impacts and other costs, determines is achievable for such source or modification through application of production processes or available methods, systems, and techniques, including fuel cleaning or treatment or innovative fuel combustion techniques for control of such pollutant.[13] An emission limitation (including a visible emission standard) based on the maximum degree of reduction for each pollutant subject to regulation under the [Clean Air] Act which would be emitted from any proposed major stationary source or major modification which the Administrator, on a case-by-case basis, taking into account energy, environmental, and economic impacts and other costs, determines is achievable for such source or modification through application of production processes or available methods, systems, and techniques, including fuel cleaning or treatment or innovative fuel combustion techniques for control of such pollutant [8]	77, 80, 165
Best management practice (BMP)	Methods that have been determined to be the most effective, practical means of preventing or reducing pollution from nonpoint sources [8]	77
Bias	Any difference between the true value and that actually obtained due to all causes other than sampling variability.	77, 80
Bioaccumulation	General term describing a process by which chemicals are taken up by an organism either directly from exposure to a contaminated	80, 165

	medium or by consumption of food containing the chemical [5]. 1. The process whereby certain toxic substances collect in living tissues, thus posing substantial hazard to human health or the environment.[13] .	
Bioassay	Using living organisms to measure the effect of a substance, factor, or condition	80
Bioavailability	The degree to which an agent is capable of being absorbed by an organism and available for metabolism or interaction with biologically significant receptors. Bioavailability involves both release from a medium (if present) and absorption by an organism.	77
Bioconcentration / Bioconcentration factor (BCF)	Bioaccumulation is the process by which chemicals concentrate in an organism. For example, DDT concentrates in fish and birds that eat fish. This concentration effect is expressed as the ratio of the concentration of the chemical in an organism (like a fish) to its The tendency of a chemical to accumulate in a living organism to levels in excess of the concentration in its surrounding environment. **Bioconcentration factor (BCF)** – provides a measure of the extent of chemical partitioning at equilibrium between a biological medium such as fish tissue or plant tissue and an external medium such as water. The higher the BCF, the greater the likely accumulation in living tissue.	48
Biological half-life	The time required for a biological system (such as a human or animal) to eliminate, by natural processes, half the amount of a substance (such as a radioactive material) that has been absorbed into that system indicators of exposure study [13]. Refers to the process whereby certain substances such as pesticides or heavy metals move up the food chain, work their way into rivers or lakes, and are eaten by aquatic organisms such as fish, which in turn are eaten by large birds, animals or humans. The substances become concentrated in tissues or internal organs as they move up the chain [8]	77, 80
Biological indicator	Species or group of species which is representative and typical for a specific status of an ecosystem, which appears frequently enough to serve for monitoring and whose population shows a sensitive response to changes, e.g. the appearance of a pesticide in the ecosystem.	14
Biological magnification (biomagnification)	The concentration of certain substances up a food chain. A very important mechanism in concentrating pesticides and heavy metals in organisms such as fish.	80
Biological monitoring (syn. Biological control)	Analyzing chemicals, hormone levels or other substances in biological materials (blood, urine, breath, etc.) as a measure of chemical exposure, health status, etc. in humans or animals. A	66

	blood test for lead is an example of biological monitoring.	
Biologically Based Dose Response (BBDR) model	A predictive model that describes biological processes at the cellular and molecular level linking the target organ dose to the adverse effect.	165
Biomarker (biological marker)	Indicator (molecular, biochemical, cellular or organism) signalling an event or condition in a biological system or sample and giving a measure of exposure to, effect of, or susceptibility to, a xenobiotic.	36
Biota	The sum total of the living organisms of any designated area	80
Biotransformation	Conversion of the chemical structure of a pesticide catalysed by enzymes ***in*** uitro or in ***viuo.*** See also ***biodegradation.***	36
Bmi:	Body mass index A measure of underweight and overweight calculated as weight (kg) divided by height squared (m2).	27
BMDL (A lower one-sided confidence limit on the BMD) Or BMCL (A lower one-sided confidence limit on the BMC).	A statistical lower confidence limit on the dose or concentration at the BMD or BMC, respectively.	125
Body burden	The total amount of a specific substance (for example, lead) in an organism, including the amount stored, the amount that is mobile, and the amount absorbed .	80
Bounding estimate	An estimate of exposure, dose, or risk that is higher than that incurred by the person with the highest exposure, dose or risk in the population being assessed. Bounding estimates are useful in developing statements that exposures, doses, or risks are "not greater than" the estimated value.	50
Burden of disease(s)	The total significance of disease for society beyond the immediate cost of treatment. It is measured in years of life lost to ill health as the difference between total life expectancy and disability-adjusted life expectancy.	183

Term	Definition	Ref.
cancer	An abnormal, potentially unlimited, disorderly new tissue growth	80
carcinogen	A substance or agent that produces or incites cancerous growth	80
carcinogenesis	Development of carcinoma; or, in more recent usage, producing any kind of malignancy. [13]. The formation of tumors caused by chemical exposures. (Very likely a series of steps). The carcinogenic event modifies the genome and/or other molecular control mechanisms in the target cells such that these can give rise to a population of altered cells. The formation of benign and	80, 12

	malignant tumors (i.e., cancers) is often considered together in determining a dose-response relationship and estimating a risk value for this endpoint. These effects are often considered not to have a threshold in response [14]	
carcinogenic	Cancer causing. A carcinogen is any agent, chemical, physical or biological, that can act on living tissue in such a way as to cause a malignant neoplasm. More simply, a carcinogen is any substance which causes cancer. A substance determined to be cancer-producing or potentially cancer-producing by IARC, NIP, OSHA, the International Agency for Research on Cancer, or the National Toxicology Program and other organizations (CalEPA - OEHHA, ACGIH, Health Canada, OECD, EC).	80
carcinogenic potency (syn. slope factor (см.), carcinogenic potency slope	The gradient of the dose-response curve for a carcinogen factor)	80
CAS (Chemical Abstracts Service registry number)	The Chemical Abstract Services unique number for each chemical. It can be used to search for a specific chemical regardless of the choice of chemical name [124]. An organization from Columbus, Ohio, which indexes information published in Chemical Abstracts by the American Chemical Society and provides index guides by which information about particular substances may be located in the Abstracts when needed. CAS numbers identify specific chemicals [8]. On **Aug 9 06:49:51 EDT 2006 CAS registry 29 355 200** organic and inorganic substances **57 742 518** sequences	27, 77
case-control study	An inquiry in which groups of individuals are selected in terms of whether they do (the cases) or do not (the controls) have the disease of which the etiology is to be studied, and the groups are then compared with respect to existing or past characteristics judged to be of possible relevance to the etiology of the disease [13]. Case-control study A study in which the risk factors of people with a disease are compared with those without a disease [59]. Case control studies select subjects based on their disease status. The study population is comprised of individuals that are disease positive, while the controls are disease negative. The case control study then looks back through time at potential exposures these populations may have encountered. A 2x2 table is constucted, displaying the individuals that are disease positive and exposure positive (A), disease positive and exposure negative (B), disease negative and exposure positive (C), and disease negative and exposure negative (D). The statistic generated to measure association is the odds ratio (OR), which is the cross product of AD/BC. If the OR is greater than 1, then the conclusion is the	18, 80

	"those with the disease are more likely to have the exposure," wherease if it is less than 1 the exposure and disease are not associated. If the OR is far less than one, it can be said that the exposure has a protective effect against the disease. Case control studies are faster and more cost effective than longer prospective studies, but are sensative to bias such as recall bias, and also cannot show that the exposure definitely occurred before the disease.	
case-fatality rate	A ratio of the number of deaths due to a disease to the number of cases of that disease in a specified period of time. It expresses the frequency with which affected individuals die of the disease.	80
CERCLA (Comprehensive Environmental Restoration and Compensation Liability Act):	Cleanup Program focuses on human health and environmental concerns related to human health. The cleanup program is primarily carried out by EPA, working with States, on sites designated for cleanup on the NPL. Cleanup Program emphasizes local source control, prevention of further spread from sources. Cleanup Program is prohibited from "restoring" natural resources, although cleanup may prevent further injuries to natural resources.	77
chemical-specific adjustment factor (CSAF)	Default safety/uncertainty factors have been used for over 40 years to estimate health-based guidance values based on no-observed-adverse-effect levels (NOAELs) or lowest-observedadverse-effect levels (LOAELs) from studies in animals. A value of 100 is normally used by bodies such as the Joint FAO/WHO Committee on Food Additives and Contaminants (JECFA) and the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) to derive an acceptable daily intake (ADI), a tolerable daily intake (TDI) or a reference dose (RfD) for the general population based on a NOAEL or LOAEL from a chronic study in animals. The approach under which CSAFs would be used in risk assessment has been such that in the absence of data, the usual default uncertainty factor would be used. This does not necessarily mean that the default of 100 is the ideal value; it is simply recognition that this reflects the common current approach to deriving a health-based guidance value for the general population. CSAF contains: INTERSPECIES DIFFERENCES - toxicodinamic (ADUF with default value 2,5), TOXICOKINETIC (AKuf with default value 4,0); INTERINDIVIDUAL DIFFERENCES: toxicodinamic (HDuf with default value 3,16) and TOXICOKINETIC (HKuf with default value 3,16).	51
chronic	Having a persistent, recurring or long-term nature. As distinguished from acute.	80
chronic effect	An adverse effect on a human or animal in which symptoms recur frequently or develop slowly over a long period of time.	77
chronic exposure	Multiple exposures occurring over an extended period of time, or a significant fraction of the animal's or the individual's life-time.	77

chronic hazard or toxicity	**Chronic Toxicity:** The capacity of a substance to cause long-term poisonous human health effects	77
chronic study/ chronic exposure	A continuous or intermittent long-term contact between an agent and a target.	50
classification of carcinogens	The organizations listed on ITER use a specific approach to classifying the human potential for carcinogenicity from exposure to a chemical. While most of these organizations are based on information from all routes of exposure and are not route-specific, EPA assessments completed after approximately 1996 may have route-specific classifications, depending on the available data and the chemical's mode of action. IARC cancer classification groups and detailed descriptions of these groups can be found in the Preamble to each monograph and at http://monographs.iarc.fr/monoeval/eval.html. Briefly, these are Group 1 - carcinogenic to humans, Group 2A - probably carcinogenic to humans, Group 2B - possibly carcinogenic to humans, Group 3 - not classifiable as to carcinogenicity, and Group 4 - probably not carcinogenic to humans. The IARC evaluation considers the evidence of carcinogenicity in humans, the evidence of carcinogenicity in experimental animals, and other data relevant to the evaluation of carcinogenicity and its mechanisms. Health Canada classifies chemicals into six groups on criteria modified from those of the International Agency for Research on Cancer (IARC): I-Carcinogenic to Humans; II-Probably Carcinogenic to Humans; III-Possibly Carcinogenic to Humans; IV-Unlikely to be Carcinogenic to Humans; V-Probably Not Carcinogenic to Humans; and VI-Unclassifiable with Respect to Carcinogenicity in Humans. More information regarding Health Canada's classification scheme can be found in Meek ME, Newhook R, Liteplo RG, Armstrong VC. 1994. Approach to assessment of risk to human health for Priority Substances under the Canadian Environmental Protection Act. In: Environmental Carcinogenesis and Ecotoxicology Review, Part C of Journal of Environmental Science and Health. C12(2):105-134. U.S. EPA published the following system in their 1986 risk assessment guidelines: A-Human Carcinogen; B-Probable human carcinogen; B1-limited evidence of carcinogenicity in humans; B2-sufficient evidence of carcinogenicity in animals with inadequate or lack of evidence in humans; C-Possible human carcinogen; D-Not Classifiable as to Human Carcinogenicity; E-Evidence of Noncarcinogenicity for Humans. In 2005 U.S. EPA in risk assessment risk of carcinogen Guideline introduce following	12

	terms: Five standard weight-of-evidence descriptors are used as part of the narrative. The suggested descriptive terms are follows: 1). Carcinogenic to humans; 2). Likely to be carcinogenic to humans 3).Suggestive evidence of carcinogenic potential; 4). Inadequate information to assess carcinogenic potential; 5(. Not likely to be carcinogenic to humans Beginning in 1996, EPA has been revising its carcinogen risk assessment guidelines to focus on mode of action and a weight of evidence narrative summarizing the chemical's carcinogenic potential. From 1996 to 1999, the following major narrative descriptors were used, with sub-descriptors in each group: "Known/likely;" "cannot be determined;" and "not likely." Beginning in approximately 1999, EPA has used the following standard hazard descriptors: "carcinogenic to humans," "likely to be carcinogenic to humans," "suggestive evidence of carcinogenic potential," "inadequate information to assess carcinogenic potential," and "not likely to be carcinogenic to humans." Depending on the chemical's mode of action, different descriptors may apply for different routes or under different exposure conditions (e.g., different doses, different co-exposures). These descriptors were finalized in the 2005 guidelines. Documents prepared by NSF International use the most recent version of the U.S. EPA guidelines for carcinogen risk assessment in classifying the human carcinogenic potential of a chemical. This is currently the U. S. EPA (2005) final guidelines, but previous risk assessments have used the U.S. EPA (1999) draft, U.S. EPA (1996) proposed, or U.S. EPA (1986) final guidelines for carcinogen risk assessment. If another agency has classified the carcinogenic potential of the chemical, that classification is noted in the risk comparisons and conclusions section of the NSF International document, with discussion if there are differences in classification. ACGIH classification: A1 - confirmed human carcinogen; A2 - suspected human carcinogen ; A3 - animal carcinogen ; A4 - not classifiable as a human carcinogen ; A5 - not suspected as a human carcinogen . OECD proposed classification: Class 1: Known or presumed carcinogen. Subclass 1A: known human carcinogen based on human evidence; Subclass 1B: presumed human carcinogen based on demonstrated animal carcinogenicity. Class 2: - suspected carcinogen; - limited evidence of human or animal carcinogenicity.	
Cleanup	Actions taken to deal with a release or threat of release of a hazardous substance that could affect humans and/or the environment. The term "cleanup" is sometimes used interchangeably with the terms remedial action, removal action,	77

	response action, or correctiv action	
CODMOD:	Cause of death model A statistical model for the prediction of the broad distribution of causes of death on observed historical data on the relationships between cause distributions, and overall levels of mortality and per-capita income.	27
coefficient of haze (COH)	A measurement of visibility interference in the atmosphere.	80
cohort study	An epidemiologic study that observes subjects in differently exposed groups and compares the incidence of symptoms. Although ordinarily prospective in nature, such a study is sometimes carried out retrospectively, using historical data. See prospective study	77, 80
Common Mechanism of Toxicity	Common mechanism of toxicity pertains to two or more pesticide chemicals or other substances that cause a common toxic effect(s) by the same, or essentially the same, sequence of major biochemical events (i.e., interpreted as mode of action). Hence, the underlying basis of the toxicity is the same, or essentially the same, for each. Two or more chemicals or other substances that cause a common toxic effect(s) by the same, or essentially the same, sequence of major biochemical events (i.e., interpreted as mode of action).	118
Common mode failures	Several errors in a technological system occurring simultaneously	80
Community	An assemblage of populations of different species within a specified location in space and time.	124
Comparative Effect Level (CEL)	A dose by which potency of chemicals may be compared; e.g. the dose causing a maximum of 15% cholinesterase inhibition.	118
comparative risk	1. An expression of the risks associated with two (or more) actions leading to the same goal; may be expressed quantitatively (a ratio of 1.5) or qualitatively (one risk greater than another risk). 2. Any comparison among the risks of two or more hazards with respect to a common scale.	80
Comparative Risk Assessment	A process that generally uses a professional judgment approach to evaluate the relative magnitude of effects and set priorities among a wide range of environmental problems (e.g., U.S. EPA, 1993d). Some applications of this process are similar to the problem formulation portion of an ecological risk assessment in that the outcome may help select topics for further evaluation and help focus limited resources on areas having the greatest risk reduction potential. In other situations, a comparative risk	124

	assessment is conducted more like a preliminary risk assessment. For example, EPA's Science Advisory Board used professional judgment and an ecological risk assessment approach to analyze future ecological risk scenarios and risk management alternatives [40]	
Compensatory Effect	This effect maintains overall function without enhancement or significant cost. Increased respiration due to metabolic acidosis is an example of a compensatory effect.	12
concentration ratio	The ratio of the concentration of a compound or radionuclide in an organism or its tissues to the concentration in the surrounding under equilibrium, or steady-state conditions.	77, 80
concentration-effect relationship	a diagram or written description of the predicted key relationships between the stressor(s) and the assessment endpoint(s) for a risk assessment. Relationship between the exposure, expressed in concentration, of a given organism, system or (sub) population to an agent in a specific pattern during a given time and the magnitude of a continuously-graded effect to that organism, system or (sub) population. Related terms: *Effect Assessment, Dose-Response Relationship[26].* Link between the exposure of a given system to a substance over time and the magnitude of a specific, continuously graded change to that system [11]	21, 55
Conceptual model	**Conceptual model**—A conceptual model in problem formulation is a written description and visual representation of predicted relationships between ecological entities and the stressors to which they may be exposed [40].	124
Concurrent Exposure	is interpreted as potential human exposure by all relevant pathways, durations, and routes that allows one chemical to add to the exposure of another chemical such that the total risk is an estimate of the sum of the exposures to the individual chemicals. This includes simultaneous exposures as well as any sequential exposures that could contribute to the same joint risk, either by overlapping internal doses or by overlapping toxic effects.	149
confidence interval	A range of values (a1 < a < a2) determined from a sample of definite rules so chosen that, in repeated random samples from the hypothesized population, an arbitrarily fixed proportion of that range will include the true value, x, of an estimated parameter. The limits, a1 and a2, arecalled confidence limits; the relative frequency with which these limits include a is called the confidence coefficient; and the complementaryprobability is called the confidence level. As with significance levels, confidence levels are commonly chosen as 0.05 or 0.01, the corresponding confidence coefficients being 0.95 or 0.99. Confidence intervals should not be interpreted as implying that the parameter itself	77, 80

	has a range of values; it has only one value, a. On the other hand, the confidence limits (a1, a2) being derived from a sample, are random variables, the values of which on a particular sample either do or do not include the true value a of the parameter. However, in repeated samples, a certain proportion of these intervals will include a provided that the actual population satisfied the initial hypothesis.	
confounding factors	Variables that may introduce differences between cases and controls which do not reflect differences in the variables of primary interest.	77, 80
contamination	Contact with an admixture of an unnatural agent, with the implication that the amount is measurable	77, 80
control group (or Reference Group):	A group used as the baseline for comparison in epidemiologic studies or laboratory studies. This group is selected because it either lacks the disease of interest (case-control group) or lacks the exposure of concern (cohort study).	125
cost-benefit analysis	A formal quantitative procedure comparing costs and benefits of a proposed project or act under a set of preestablished rules. To determine a rank ordering of projects to maximize rate of return when available funds are unlimited, the quotient of benefits divided by costs is the appropriate form; to maximize absolute return given limited resources, benefits-costs is the appropriate form. **Cost-benefit-risk assessment**" is the quantification and monetary valuation of the expenditures, gains, and losses, and the calculation of net benefits to society associated with the adoption of a particular regulation (or alternative management strategy) to address an environmental hazard. *Quantitative environmental risk analysis (that is, risk assessment) is a necessary prerequisite to the conduct of cost-benefit-risk assessment of environmental regulations,* because the " **benefits**" are the risks avoided (that is, the adverse effects on human health or the environment, or risks of such effects, that the regulation is meant to address.) Risk assessment may be used to estimate the number of people or animals likely to be harmed by exposure to the hazard under each regulatory strategy, including a "do-nothing-different" strategy that reflects the current policy, or regulation, or laissez faire. Benefits may be expressed in such terms as numbers of lives saved or illnesses or species extinctions avoided. Risk that is expected to remain after a new regulation is implemented may be subtracted from the risk under current conditions to estimate risk reduction opportunities -- that is, the "**expected benefit** " -- of each regulatory alternative. If benefits are translated into monetary terms to allow cost-benefit-risk assessment, various techniques may be used to calculate the dollar values of health effects; these values may be derived from studies of how much	77, 80

	people are willing to pay to avoid exposure to a hazard or particular adverse effect, or based on savings of direct costs, such as health care expenditures, salary loss for the duration of an illness, or the years of work lost to premature death. The intent is to estimate the gross monetary value of benefits to society, rather than to individuals. "**Net benefit**" is the expected monetary benefit less the cost of implementing the regulation.	
Cost-Effective Alternative	An alternative control or corrective method identified after analysis as being the best available in terms of reliability, performance, and cost. Although costs are one important consideration, regulatory and compliance analysis does not require EPA to choose the least expensive alternative. For example, when selecting or approving a method for cleaning up a Superfund site the Agency balances costs with the long-term effectiveness of the methods proposed and the potential danger posed by the site.	77
CR(inhal)	The cancer risk from inhalation exposure, CR(inhal) is the 1 in 10,000 (E-4) lifetime excess cancer risk following exposure by inhalation (expressed in microgram/cu.m), as derived by RIVM. For comparison purposes on *ITER*, this value has been converted to a 1 in 100,000 (E-5) risk level, and has also been converted to milligrams/cu.m.	12
CR(oral)	The cancer risk from oral exposure, CR(oral) is the 1 in 10,000 (E-4) lifetime excess cancer risk following oral exposure (expressed in microgram/kg bw-day), as derived by RIVM. For comparison purposes on *ITER*, this value has been converted to a 1 in 100,000 (E-5) risk level, and has also been converted to milligrams/kg-day.	12
criteria	As used in the Clean Air Act, information on adverse effects of air pollutants on human health or the environment at various concentrations. The information is collected pursuant to section 108 of the Clean Air Act and used to set national ambient air quality standards.	80
criteria pollutants	The 1970 amendments to the Clean Air Act required EPA to set National Ambient Air Quality Standards for certain pollutants known to be hazardous to human health. EPA has identified and set standards to protect human health and welfare for six pollutants: ozone, carbon monoxide, total suspended particulates, sulfur dioxide, lead, and nitrogen oxide. The term, "criteria pollutants" derives from the requirement that EPA must describe the characteristics and potential health and welfare effects of these pollutants. It is on the basis of these criteria that standards are set or revised.	77
Critical Concentration	An ambient chemical concentration expressed in units of µg/m3 and used in the operational derivation of the inhalation RfC. This concentration will be the NOAEL Human Equivalent Concentration	125

	(HEC) adjusted from principal study data.	
critical effect	The first adverse effect, or its known precursor, that occurs as the dose rate increases. There is an assumption that for some toxic responses, there is a level (threshold) below which adverse effects will not occur. The critical effect is often the basis of noncancer risk values, on the assumption that if the critical effect is prevented, then all subsequent adverse effects are prevented.	12
critical organ	That part of the body that is most susceptible to radiation damage under the specific conditions under consideration.	80
critical toxic effect	The most sensitive and specific biological change which is outside of acceptable physiological variation	80
cross-sectional study	An epidemiological study design in which measurements of cause and effect are made at the same point in time.	77
cumulative dose	The amount of multiple (two or more) substances which share a common mechanism of toxicity available for interaction with biological targets from multiple routes of exposure.	176
cumulative exposure assessment	A process for developing an estimate of the extent to which a defined population is exposed to two or more chemicals which share a common mechanism of toxicity by all relevant routes and from all relevant sources.	176
cumulative impacts	the sum of all individual impacts occurring over time and space, including those of the foreseeable future [2]**.** The combination of aggregate exposures to multiple agents or stressors [44].	137
cumulative ecological risk assessment	A process that involves consideration of the aggregate ecological risk to the target entity caused by the accumulation of risk from multiple stressors.	124
cumulative effects	1) the sum of all environmental effects resulting from cumulative impacts and 2) the combination of effects from all pesticide chemical residues which have a common mechanism of toxicity (Food Quality Protection Act, 1996).	137
ecological entity	A general term that may refer to a species, a group of species, an ecosystem function or characteristic, or a specific habitat. An ecological entity is one component of an assessment endpoint [40].	124
ecological relevance	One of the three criteria for assessment endpoint selection. Ecologically relevant endpoints reflect important characteristics of the system and are functionally related to other endpoints.	124
cumulative risk	is the risk of a common toxic effect associated with concurrent exposure by all relevant pathways and routes of exposure to a group of chemicals that share a common mechanism of toxicity.	149
cumulative risk assessment	involves the consideration of the aggregate ecologic or human health risk to the target entity caused by the accumulation of risk from multiple stressors, [multiple pathways, sources][2]. For the	7, 118, 124,

	purpose of implementation of FFDCA as amended by FQPA, cumulative risk is the likelihood for the cumulation of a common toxic effect resulting from all pathways and routes of exposure to substances sharing a common mechanism of toxicity[42]. The process that evaluates the likelihood that adverse ecological effects may occur or are occurring as a result of exposure to one or more stressors [40].	137
cumulative toxicity or toxic effect	A cumulative toxic effect(s) is the net change in magnitude of a common toxic effect(s) resulting from exposure to two or more substances that cause the common toxic effect(s) from a common mechanism, relative to the magnitude of the common toxic effect(s) caused by exposure to any of the substances individually.	118
damage	Damage is the severity of injury or the physical, functional, or monetary loss that could result if control of a hazard is lost.	125, 182
danger	Expresses a relative exposure to a hazard. A hazard may be present, but there may be little danger because of the precautions taken.	80
default values	Default value: pragmatic, fixed or standard value used in the absence of relevant data.	47
degradation	Physical, metabolic, or chemical change to a less complex form.	80
de minimis risk	From the legal maxim "de minimis non curat lex" or "the law is not concerned with trifles."	80
deposition	1. The laying down or precipitation of mineral matter that may eventually form rocks or that creates secondary land forms such as deltas and sand dunes. 2. The transfer of substances in air to surfaces, including soil, vegetation, surface water, or indoor surfaces, by dry or wet processes	80
dermal	Contact between a chemical and the skin. Dermal Adsorption: The process by which materials come in contact with the skin surface, but are then retained and adhered to the permeability barrier without being taken into the body.	77
deterministic Effect	The health effects, the severity of which varies with the dose and for which a threshold is believed to exist. Radiation-induced cataract formation is an example of a deterministic effect (also called a non-stochastic effect) (see 10 CFR 20.1003) [8]. This approach to risk assessment uses point estimates, for example, single maximum values or average values, to represent input variables in an exposure model. This can be compared to a probabilistic approach which considers the full range of potential exposures incurred by members of a population.	77
developmental toxicity	Adverse effects on the developing child which result from exposure to toxic chemicals or other toxic substances. Adverse effects can include birth defects, low birth weight, and functional or behavioral weaknesses that show up as the child develops.	127

	Developmental toxicology – The study of adverse effects on the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the lifespan of the organism. The major manifestations of developmental toxicity include: (1) death of the developing organism, (2) structural abnormality, (3) altered growth, and (4) functional deficiency. Any adverse effects induced prior to attainment of adult life, including effects induced or manifested in the embryonic or fetal period and those induced or manifested postnatally (before sexual maturity). OECD proposed follow classification development toxicants: 1: known or presumed human reproductive or developmental toxicant Class 1A: Known Class 1B:presumed.. Class 2: suspected human reproductive toxicant; Additional Class: effects on or via lactation	
disabling injury	An injury causing death, permanent disability, or any degree of temporary total disability beyond the day of the accident.	80
disability	Restriction or lack of ability (resulting from an impairment or health condition) to perform an activity in the manner or within the range considered normal. Although the word "disability" is widely used, the ICF (q.v.) uses this term only as a broad umbrella term for capacity and performance in activity/participation domains. The GBD (q.v.) used the term disability, as in the DALY (q.v.), as a synonym for health state (q.v.) less than full health (q.v.). Disability is also commonly used to refer only to long-standing limitations in carrying out activities of daily living.	7
disability-free life expectancy (DELE)	A form of HE (q.v.) which gives a weight of 1 to states of health with no disability above an explicit or implicit threshold and a weight of 0 to states of health with any level of disability above that threshold.	7
disability weight	Measure of the relative valuations of a health state on an interval scale. In the GBD (q.v.), health state valuations lie between 0 (full health q.v.) and 1 (state equivalent to death). The disability weight quantifies judgments about overall levels of health associated with different health states (q.v.), not judgments on the relative values of lives lived, persons, or of overall well-being, quality of life or utility. The GBD disability weights are intended to reflect average global valuations.	7
discounting	Process applied to costs, benefits, and outcomes based on the concept that there is preference for money health in the present relative to the future. · **Discounting.** One of the problems that arises in developing a benefit-cost analysis is that the benefits and costs often occur in different time periods. When this occurs, it is not appropriate, when comparing benefits and costs, to simply add up the benefits and costs accruing over time.	7

	Discounting takes account of the fact that resources (goods or services) that are available in a given year are worth more than the identical resources available in a later year. One reason for this is that resources can be invested so as to return more resources later. In addition, people tend to be impatient and to prefer earlier consumption over later consumption. a. Basic considerations. Constant-dollar benefits and costs must be discounted to present values before benefits and costs in different years can be added together to determine overall net benefits. To obtain constant dollar estimates, benefit and cost streams in nominal dollars should be adjusted to correct for inflation. The basic guidance on discount rates for regulatory and other analyses is provided in OMB Circular A-94. The discount rate specified in that guidance is intended to be an approximation of the opportunity cost of capital, which is the before-tax rate of return to incremental private investment. The Circular A-94 rate, which was revised in 1992 based on an extensive review and public comment, reflects the rates of return on low yielding forms of capital, such as housing, as well as the higher rates of returns yielded by corporate capital. This average rate currently is estimated to be 7 percent in real terms (i.e., after adjusting for inflation). As noted in the A-94 guidance, agencies may also present sensitivity analyses using other discount rates, along with a justification for the consideration of these alternative rates. The economic analysis also should contain a schedule indicating when all benefits and costs are expected to occur. In general, the discount rate should not be adjusted to account for the uncertainty of future benefits and costs. Risk and uncertainty should be dealt with according to the principles presented in Section 4 below and not by changing the discount rate. Even those benefits and costs that are hard to quantify in monetary terms should be discounted. The schedule of benefits and costs over time therefore should include benefits that are hard to monetize. In many instances where it is difficult to monetize benefits, agencies conduct regulatory "cost-effectiveness" analyses instead of "net benefits" analyses. When the effects of alternative options are measured in units that accrue at the same time that the costs are incurred, annualizing costs is sufficient and further discounting of non-monetized benefits is unnecessary; for instance, the annualized cost	

per ton of reducing certain polluting emissions can be an appropriate measure of cost-effectiveness. However, when effects are measured in units that accrue later than when the costs are incurred, such as the reduction of adverse health effects that occur only after a long period of exposure, the annualized cost per unit should be calculated after discounting for the delay between accrual of the costs and the effects.

In assessing the present value of benefits and costs from a regulation, it may be necessary to consider implications of changing relative prices over time. For example, increasing scarcity of certain environmental resources could increase their value over time relative to conventional consumer goods. In such a situation, it is inappropriate to use current relative values for assessing regulatory impacts. However, while taking into account changes over time in relative values may have an effect similar to discounting environmental impacts at a lower rate, it is important to separate the effects of discounting from the effects of relative price changes in the economic analysis. In particular, the discount rate should not be adjusted for expected changes in the relative prices of goods over time. Instead, any changes in relative prices that are anticipated should be incorporated directly in the calculations of benefit and cost streams.

b. Additional considerations. Modern research in economic theory has established a preferred model for discounting, sometimes referred to as the shadow price approach. The basic concept is that economic welfare is ultimately determined by consumption; investment affects welfare only to the extent that it affects current and future consumption. Thus, any effect that a government program has on public or private investment must be converted to an associated stream of effects on consumption before being discounted.

Converting investment-related benefits and costs to their consumption-equivalents as required by this approach involves calculating the "shadow price of capital." This shadow price reflects the present value of the future changes in consumption arising from a marginal change in investment, using the consumption rate of interest (also termed the rate of time preference) as the discount rate. The calculation of the shadow price of capital requires assumptions about the extent to which government actions -- including regulations -- crowd out

private investment, the social (i.e., before-tax) returns to this investment, and the rate of reinvestment of future yields from current investment.

Estimates of the shadow price are quite sensitive to these assumptions. For example, in some applications it may be appropriate to assume that access to global capital markets implies no crowding out of private investment by government actions or that monetary and fiscal authorities determine aggregate levels of investment so that the impact of the contemplated regulation on total private investment can be ignored. Alternatively, there is evidence that domestic saving affects domestic investment and that regulatory costs may also reduce investment. In these cases, more substantial crowding out would be an appropriate assumption.

The rate of time preference is also a complex issue. Generally, it is viewed as being approximated by the real return to a safe asset, such as Government debt. However, a substantial fraction of the population does little or no saving and may borrow at relatively high interest rates.

While the shadow price approach is theoretically preferred, there are several practical challenges to its use. Agencies wishing to use this methodology should consult with OMB prior to doing so, and should clearly explain their solutions to the methodological and empirical challenges noted above.

c. Intergenerational analysis. Comparisons of benefits and costs across generations raise special questions about equity, in addition to conventional concerns about efficiency. One approach to these questions is to follow the discounting procedures described above and to address equity issues explicitly rather than through modification of the discount rate.

An alternative approach is to use a special social rate of time preference when conducting intergenerational analyses in order to properly value changes in consumption in different generations. For example, one philosophical perspective is that the social marginal rate of substitution between the well-being of members of successive generations may be less than the individual rate of time preference, and that future generations should not have their expected welfare discounted just because they come later in time. Instead, this view suggests that discounting should reflect only

	the growth of per capita consumption and the corresponding decrease in marginal utility over time. As this approach uses a consumption-based rate of interest, costs and benefits must also be adjusted to reflect the shadow price of capital. As in other cases when agencies seek to use the shadow price of capital approach, they should consult with OMB prior to conducting special analyses of regulations having substantial intergenerational effects.	
Disease	A general term describing a morbid condition which can be defined by objective, physical signs (e.g. hypertension), subjective symptoms or mental phobias, disorder of function (e.g. biochemical abnormality), or disorders of structure (anatomic or pathological change) . Existence of disease may be questioned in disorder of structure without associated disorder of function.	80
DisMod	An epidemiological disease model linking populations exposed to risk of disease with incident cases, prevalent cases, case fatality and the duration of time lived with a disease or injury, including its sequelae.	7
diversity	Pertaining to the variety of species within a given association of organisms. Areas with low diversity are characterized by a few species; often relatively large numbers of individuals represent each species.	80
dose	The amount or concentration of undesired matter or energy deposited at the site of effect. See also absorbed dose [13].Total amount of an agent administered to, taken up or absorbed by an organism, system or (sub) population [26]. total amount of a substance administered to, taken, or absorbed by an organism[11]. The amount of substance available for interaction with metabolic processes or biologically-significant receptors after crossing the outer boundary of an organism [42].	21, 55, 80, 118
dose additivity	is the Agency's assumption when evaluating the joint risk of chemicals that are toxicologically similar and act at the same target site. In other words, it is assumed that each chemical behaves as a concentration or dilution of every other chemical in the CAG (or chemical mixture). The response of the combination is the response expected from the equivalent dose of an index chemical. The equivalent dose is the sum of the component doses, scaled by each chemical's toxic potency relative to the index chemical [43]. *Dose Additivity* – When each chemical behaves as a concentration or dilution of every other chemical in the mixture. The response of the combination is the response expected from the equivalent dose of an index chemical. The equivalent dose is the sum of component doses scaled by their toxic potency relative to the index chemical [109].	131, 149
dose-effect	The relationship between dose (usually an estimate of dose) and the gradation of the effect in a population, that is a biological	80

	change measured on a graded scale of severity, although at other times one may only be able to describe a qualitative effect that occurs within some range of exposure levels.	
dose-effect relationship	Relationship between the total amount of an agent administered to, taken up or absorbed by an organism, system or (sub) population and the magnitude of a continuously-graded effect to that organism, system or (sub)population . Related terms: *Effect Assessment, Dose-Response Relationship, Concentration-Effect Relationship* [26]. Link between the total amount of a substance administered, taken, or absorbed by a system and the magnitude of a specific, continuously graded change affecting it. Related term: effect assessment below[11]	21, 55
dose-rate	Dose per unit time (e.g., mg/day). Also called dosage. Dose rates are often expressed on a per-unit-body-weight basis (mg/kg/day). Dose rates may also be expressed as an average over a time period (i.e., lifetime).	50, 118
dose-related effect	Any effect to an organism, system or (sub) population as a result of the quantity of an agent administered to, taken up or absorbed by that organism, system or (sub) population[26]. **dose-related effect**: change to a system as a function of the quantity of a substance administered, taken, or absorbed by it[11]	21, 55
dose-response	The relationship between dose (usually an estimate of dose) and the gradation of the effect in a population, that is a biological change measured on a graded scale of severity, although at other times one may only be able to describe a qualitative effect that occurs within some range of exposure levels [13]. Relationship between the amount of an agent administered to, taken up or absorbed by an organism, system or (sub) population and the change developed in that organism, system or (sub) population in reaction to the agent. Synonymous with Dose-response relationship. Related Term: *Dose-Effect Relationship, Effect Assessment, Concentration-Effect Relationship*.	55, 80
dose-response assessment	The process of characterizing the relation between the dose of an agent administered or received and the incidence of an adverse health effect in exposed populations and estimating the incidence of the effect as a function of human exposure to the agent [13]. Analysis of the relationship between the total amount of an agent administered to, taken up or absorbed by an organism, system or (sub)population and the changes developed in that organism, system or (sub)population in reaction to that agent, and inferences derived from such an analysis with respect to the entire population. Dose-Response Assessment is the second of four	21, 55

	steps in risk assessment[26]. The second of four steps in risk assessment, consisting of the analysis of the relationship between the total amount of an agent absorbed by a group of organisms and the changes developed in the group in reaction to the agent, and inferences derived from such an analysis with respect to the entire population [11] Related terms: *Hazard Characterisation, Dose-Effect Relationship, Effect* *Assessment, Dose-Response Relationship, Concentration-Effect Relationship*.[26]	
dose-response curve	Graphical presentation of a dose-response relationship [26]. Graphical presentation of a dose-response relationship [11].	21, 55
dose-response relationship	Relationship between the amount of an agent administered to, taken up or absorbed by an organism, system or (sub) population and the change developed in that organism, system or (sub) population in reaction to the agent. Related Term: *Dose-Effect Relationship, Effect Assessment, Concentration-Effect Relationship*[26]. Link between the amount of an agent absorbed by a population and the change developed in that population in reaction to it. Note: It may be expressed as the proportion of a population exposed to an agent that shows a specific reaction. It may also be used to signify the magnitude of an effect in one organism (or part of an organism); in that case, it is more specifically called "dose-effect relationship" [11]	55
dust	Fine grain particles light enough to be suspended in air	80

Term	Definition	Ref.
ecological fallacy	The inference that a correlation between variables derived from data grouped in social or other aggregates (ecological units) will hold between persons (individual units).[8]. The inference that a correlation between variables derived from data grouped in social or other aggregates (ecological units) will hold between persons (individual units).[13]. The ecological fallacy consists in thinking that relationships observed for groups necessarily hold for individuals: if countries with more Protestants tend to have higher suicide rates, then Protestants must be more likely to commit suicide; if countries with more fat in the diet have higher rates of breast cancer, then women who eat fatty foods must be more likely to get breast cancer. These inferences may be correct, but are only weakly supported by the aggregate data. Innappropriate conclusions regarding relationships at the individual level based on ecological data.	77, 80
ecological exposure	A portion of the analysis phase of ecological risk assessment that evaluates the interaction of the stressor with one or more	124

characterization	ecological entities. Exposure can be expressed as co-occurrence or contact, depending on the stressor and ecological component involved [40].	
ecological effects characterization	In this second phase of the risk assessment process, the risk assessors evaluate exposure to stressors (**exposure characterization**) and the relationship between stressor levels and ecological effects (**ecological effects characterization**). The risk assessor performs the following tasks: 1. Selects the data that will be used and determines the strengths and weaknesses of the data 2. Analyzes the sources of stressors, distribution in the environment, and potential or actual exposure to the stressors 3. Examines stressor-response relationships and the relationship between measures of effect and assessment endpoints During these analyses, the scientists evaluate the uncertainties in the exposure and effects characterizations. The products of the analysis phase are two profiles: 1. Exposure profile based on environmental fate and transport data 2. Ecological effects or stressor-response profile The risk assessors and risk managers continue to interact throughout this phase. that describes the types of effects a pesticide can produce in an organism and how those effects change with varying pesticide exposure levels. This characterization is based on an ecological effects profile (assessment) that describes the available effects (toxicity) information for various plants and animals and an interpretation of available incidents information and effects monitoring data. A portion of the analysis phase of ecological risk assessment that evaluates the ability of a stressor(s) to cause adverse effects under a particular set of circumstances [40].	124
ecological epidemiology	A branch of epidemiology which views disease as a result of the ecological interactions between populations of hosts and parasites; what we do. We contrast this with classical epidemiology. The interaction between a host and an infectious agent in the environment	164
ecological impact	The total effect of an environmental change, natural or man-made, on the community of living things.[8]. 1. The total effect of an environmental change, natural or man-made, on the	77, 80

	community of living things.[13]	
ecological indicator	A characteristic of the environment that, when measured, quantifies magnitude of stress, habitat characteristics, degree of exposure to a stressor, or ecological response to exposure. The term is a collective term for response, exposure, habitat, and stressor indicators.	77
ecological risk assessment	The application of a formal framework, analytical process, or model to estimate the effects of human action(s) on a natural resource and to interpret the significance of those effects in light of the uncertainties identified in each component of the assessment process. Such analysis includes initial hazard identification, exposure and dose response assessments, and risk characterization [8]. An **ecological risk assessment** tells what happens to a bird, fish, plant or other non-human organism when it is exposed to a stressor, such as a pesticide. Ecological risk assessment is a process that evaluates the likelihood that adverse ecological effects may occur or are occurring as a result of exposure to one or more stressors [40].	77, 124
ecology	The science dealing with the relationship of all living things with each other and with their environment.	80
ecosystem	The interacting system of a biological community and its nonliving surroundings [13]. The biotic community and abiotic environment within a specified location in space and time [40].	80, 124
effect	A biological change caused by an exposure [13]. Change in the state or dynamics of an organism, system or (sub) population caused by the exposure to an agent [26]. **effect**: change in the state or dynamics of a system caused by the action of an agent [11].	21, 55, 80
effect assessment	Combination of analysis and inference of possible consequences of the exposure to a particular agent based on knowledge of the dose-effect relationship associated with that agent in a specific target organism, system or (sub) population [26]. Combination of analysis and inference of possible consequences of the exposure to a particular substance based on knowledge of the dose-effect relationship associated with it in a specific target system [11]	21, 55
effect severity levels	U.S.EPA Severity Level Effect Category : 0 (NOEL, No observed effects. Mild Effect); 1 (NOAEL, Enzyme induction or other biochemical change, consistent with possible mechanism of action, with no pathologic changes and no change in organ weights. Mild Effect);2 (NOAEL, Enzyme induction and subcellular proliferation or other changes in organelles, consistent with possible mechanism of action, but no other apparent effects. Mild Effect); 3 (NOAEL, Hyperplasia, hypertrophy, or atrophy, but without changes in organ weight. ·Mild Effect); 4 (NOAEL/	76, 147

	LOAEL, Hyperplasia, hypertrophy, or atrophy, with changes in organ weight., Mild effect); 5(LOAEL, Reversible cellular changes including cloudy swelling, hydropic change, or fatty changes. Mild / Severe Effect); 6 ((LO)AEL Degenerative or necrotic tissue changes with no apparent decrement in organ function. Severe Effect); 7 ((LO)AEL/FEL, Reversible slight changes in organ function. Severe Effect); 8 (FEL Pathological changes with definite organ dysfunction that are unlikely to be fully reversible. Severe Effect); 9 (FEL, Pronounced pathological change with severe organ dysfunction and long-term sequelae. Severe Effect); 10 (FEL Life-shortening or death. Life-threatening)	
effective dose (ED10)	The dose corresponding to a 10% increase in an adverse effect, relative to the control response [1]. The effective dose is a measured or estimated dose level associated with some designated level or percent of response relative to the control or baseline level of response. For example, the ED10 is a dose associated with a 10% response. The effective does is essentially the same as a benchmark dose (BMD). It is determined by using a curve-fitting procedure that is applied to the dose-response data for a chemical [42].	118, 125
efficacy	A measure of the probability and intensity of beneficial effects.	77, 80
effluent	Waste material discharged into the environment, treated or untreated. Generally refers to water pollution.	77, 80
ELCR (excess lifetime cancer risk)	Potential carcinogenic effects that are characterized by estimating the probability of cancer incidence in a population of individuals for a specific lifetime from projected intakes (and exposures) and chemical-specific dose-response data (i.e., slope factors). By multiplying the intake by the slope factor, the ELCR result is a probability. The additional or extra risk of developing cancer due to exposure to a toxic substance incurred over the lifetime of an individual.	77
emergency exposure guidance Level (EEGL)	is defined by the National Academy of Sciences as the ceiling concentration of a substance in air that may be judged by the Department of Defense to be acceptable for the performance of specific tasks during rare emergency conditions lasting for periods of 1-24 hours. “Emergency” connotes an unexpected situation with potential for loss of life. EEGLs are designed to provide guidelines for military personnel operating under emergency conditions that are peculiar to military operations and for which regulatory agencies have not set standards. The methods used to derive the EEGLs are not always explicitly stated and EEGLS were not derived with the intent to protect the general public. However, the levels derived for sulfuric acid and for xylenes were deemed acceptable for use as levels protective	9

	against serious adverse effects.	
emission	Like effluent but used in regard to air pollution.	80
emission rate	The amount of pollutant emitted per unit of time.	80
environment	Water, air, land, and all plants and man and other animals living therein, and the interrelationships which exist among them	77, 80
environmental assessment:	An environmental analysis prepared pursuant to the National Environmental Policy Act to determine whether a federal action would significantly affect the environment and thus require a more detailed environmental impact statement.	77
environmental audit	An independent assessment of the current status of a party's compliance with applicable environmental requirements or of a party's environmental compliance policies, practices, and controls.	77
environmental equity	Equal protection from environmental hazards of individuals, groups or communities regardless of race, ethnicity, or economic status	7
environmental exposure characterization	that estimates the potential exposure of plants, animals, and water resources to pesticide residues in water, food, and air. This characterization includes information on how often, how long, and the amount of pesticide to which an organism may be exposed. It is based on environmental fate and transport data as well as modeling and monitoring information. As much as 24% of global disease is caused by environmental exposures which can be averted. Well-targeted interventions can prevent much of this environmental risk, the World Health Organization (WHO) demonstrates in a report issued today. The report further estimates that more than 33% of disease in children under the age of 5 is caused by environmental exposures. Preventing environmental risk could save as many as four million lives a year in children alone, mostly in developing countries [37.	177
environmental health indicators (EH indicators)	EH indicator fact-sheet model as main reporting tool and decided to prepare an international indicator-based report demonstrating the usefulness of the system for monitoring and evaluating the ongoing policies on environment and health across Europe. Main group of EH indicators: Air quality, Noise, Housing, Traffic Accidents, Water and Sanitation, Chemical Emergencies, Radiation. http://www.euro.who.int/EHindicators/indicators/20040311_1	179, 181
environmental impact assessment (EIS)	assessment required by the National Environmental Policy Act to evaluate fully potential environmental effects associated with proposed federal actions [2]. **E**nvironmental impact statements are prepared under the National Environmental Policy Act by Federal agencies as they	124, 137

	evaluate the environmental consequences of proposed actions. EISs describe baseline environmental conditions; the purpose of, need for, and consequences of a proposed action; the no-action alternative; and the consequences of a reasonable range of alternative actions. A separate risk assessment could be prepared for each alternative, or a comparative risk assessment might be developed. However, risk assessment is not the only approach used in EISs.	
environmental impact appraisal	An environmental review supporting a negative declaration, i.e., the action is not a major Federal action significantly affecting the environment. It describes a proposed EPA action, its expected environmental impact, and the basis for the conclusion that no significant impact is anticipated.	77, 80
environmental medicine	the healthcare specialty concerned with human illnesses or dysfunctions that result from environmental factors [60]. **Environmental medicine**, also called **clinical ecology**, is a multidisciplinary field involving medicine, environmental science, chemistry and others. The scope of this field involves studying the interactions between environment and human health, the cause of disease as caused by environmental factors including chemical, physical and biological agents. Medical specialty concerned with environmental factors that may impinge upon human disease, and development of methods for the detection, prevention, and control of environmentally related disease (Webster Dictionary)	22, 168
environmental pathway	All routes of transport by which a toxicant can travel from its release site to human populations including air, food chain, and water. The connected set of environmental media through which a potentially harmful substance travels from source to receptor.	77, 80
environmental risk assessment (EnRA)	deals with the interactions of agents or hazards, humans and ecological resources. It describes human populations, ecological resources and agents, analyzes agents and exposure potential, characterizes the potential for adverse effects, defines uncertainties, generates options to deal with the risks, and communicates information about the risks to humans and ecosystems. EnRA has two components: Human Health Risk Assessment (HHRA) and Ecological Risk Assessment (EcoRA). The stages of doing an EnRA include: Hazard Identification and Problem Formulation, Analysis, and Risk Characterization. The main outputs are the risk management and communication plans. Properly used, EnRA will take its place in attaining sustainable development goals of industrialized and developing countries. "**Environmental risk assessment**" refers to any formal or informal scientific procedure used to produce a quantitative estimate of environmental risk. For example, risk assessment is often used to estimate the expected rate of illness or death in a human	90

	population ex-posed to a hazardous chemical based on the number of experimental animals affected by various doses of the chemical as measured in laboratory experiments.	
EPA (U.S.Environmental Protection Agency)	Created in 1970, the EPA is responsible for working with state and local governments to control and prevent pollution in areas of solid and hazardous waste, pesticides, water, air, drinking water, and toxic and radioactive substances	77
epidemiology	The study of the distribution and dynamics of diseases and injuries in human populations. Specifically, the investigation of the possible causes of a disease and its transmission Study of the analysis of the distribution of illnesses, physiological variables and social consequences of illnesses in human population groups, as well as factors influencing this distribution (WHO definition).	77, 80
excess death	The excess over statistically expected deaths in a population within a given time interval. Attempts are made to relate excess deaths to specific causes. Note that since every person can (and must) die only once, there can be no excess deaths over all time.	80
excess lifetime cancer risk (ELCR)	Potential carcinogenic effects that are characterized by estimating the probability of cancer incidence in a population of individuals for a specific lifetime from projected intakes (and exposures) and chemical-specific dose-response data (i.e., slope factors). By multiplying the intake by the slope factor, the ELCR result is a probability	77
excess risk	proportion of individuals or animals observed or estimated to possess an effect in addition to the spontaneous background risk. Typically, the number of estimated potential excess lifetime cancer cases occurring per million persons continuously exposed for 70 years to a given concentration of a toxic air contaminant. For example, the excess carcinogenic risk from acetaldehyde exposure is 7 to 75 potential lifetime cancer cases per million persons continuously exposed to 1 ppb acetaldehyde (7 - 75 potential lifetime cancer cases/10^6 ppb persons). In this case, 7 is the risk based on the lower bound potency and 75 is the risk based on the upper bound potency.	47
expected deaths	The number of deaths statistically expected in a population in a given time interval obtained by summing the product of age-, sex-, and race- specific mortality rates from a standard population and person-years in each age, sex, and race category in the study population.	80
expected loss	The quantity obtained by multiplying the magnitude of health or environmental effect loss by the probability (or risk) of that loss and adding the products. The expected loss is the average loss over a large number of trials; one must reflect on the appropriateness of its use in cases for which there will be only	80

	one, or a few, trials.	
expert judgment	Opinion of an authoritative person on a particular subject [11, 26].	21, 55
exposure	1. The time integral of the concentration of a toxicant which is in the immediate vicinity of various ports of entry (such as lung, GI tract and skin). 2. Qualitatively, contact between a potentially harmful agent and a receptor (e.g., a human or other organism) that could be affected [13]. Concentration or amount of a particular agent that reaches a target organism, system or (sub) population in a specific frequency for a defined duration [26]. Concentration, amount, or intensity of a particular agent that reaches a target system. It is usually expressed in numerical terms of substance concentration, duration, frequency, and intensity [11]. Contact of a substance with the outer boundary of an organism. Exposure is quantified as the concentration of the agent in the medium in contact integrated over the time duration of that contact [42] .The contact or co-occurrence of a stressor with a receptor [40]. Contact between an agent and a target. Contact takes place at an exposure point or exposure surface over an exposure interval. For inhalation and ingestion routes, exposure is expressed as a function of exposure concentration; for the dermal route, exposure is expressed as a function of exposure loading [49].	21, 50, 55, 80, 118
exposure assessment	The process of measuring or estimating the intensity, frequency, and duration of human exposures to an agent currently present in the environment or of estimating hypothetical exposures that might arise from the release of new chemicals into the environment.[13]. Evaluation of the exposure of an organism, system or (sub) population to an agent (and its derivatives). Exposure Assessment is the third step in the process of Risk Assessment [26]. Step in the process of risk assessment, consisting of a quantitative and qualitative analysis of the presence of an agent (including its derivatives) that may be present in a given environment and the inference of the possible consequences it may have for a given population of particular concern Note 1: [engineering] determination, through the use of a variety of analytical techniques, of the quantity and fate of a chemical, physical, or biological agent in a medium of concern. The process of estimating or measuring the intensity, frequency, and duration of exposure to an agent. Ideally, it describes the sources, pathways, routes, magnitude, duration, and pattern of exposure; the characteristics of the populations exposed; and the uncertainties in the assessment [49]. Exposure Contact of chemical with concentration x time **Dermal:** (mg chem/L water) (hrs of outer boundary of a person, contact) e.g., skin, nose, mouth.**Respiratory:** (ppm chem in air) (hrs of **Oral:** (mg chem/L	50, 55, 80, 118,

	water) (min of (mg chem/kg soil) (hrs of contact) contact) (µg/m air) (days of 3 contact) contact) (mg chem/kg food) (min of contact).	
exposure concentration	The concentration of a chemical in its transport or carrier medium at the point of contact [44]. The amount of agent present in the contact volume divided by the contact volume. For example, the amount of agent collected in a personal air monitor divided by volume sampled. [49]	50
exposure duration	The total time period over which contacts occur between an agent and a target. For example, if an individual is in contact with an agent for 10 minutes a day, for 300 days over a one year time period, the exposure duration is one year.	50
exposure (external)	contact of an organism with a chemical, radiological, or physical agent. Exposure is quantified as the amount of the agent available at the exchange boundaries of the organism (e.g.; skin, lungs, gut) and available for absorption	80
exposure frequency	The number of exposure intervals in an exposure duration.	50
exposure interval	A period of continuous contact between an agent and a target.	50
exposure loading	The amount of agent present in the contact volume divided by the exposure surface area. For example, a dermal exposure measurement based on a skin wipe sample, expressed as a mass of residue per skin surface area, is an exposure loading.	50
exposure pathway	The physical course a chemical or pollutant takes from its source to the organism exposed [44]. The course an agent takes from the source to the target [49]	50
exposure point concentration	The value that represents a conservative estimate of the chemical concentration available from a particular medium or route of exposure.	43
Exposure profile	The product of characterization of exposure in the analysis phase of ecological risk assessment. The exposure profile summarizes the magnitude and spatial and temporal patterns of exposure for the scenarios described in the conceptual model.	124
exposure route	The way a chemical or pollutant enters an organism after contact, e.g., by ingestion, inhalation, or dermal absorption.	50
exposure scenarios (Scenario)	Exposure scenarios are a tool to help the assessor develop estimates of exposure, dose, and risk. An exposure scenario generally includes facts, data, assumptions, inferences, and sometimes professional judgment about how the exposure takes place. The human physiological and behavioral data necessary to construct exposure scenarios can be obtained from the Exposure	21, 50, 55

	Factors Handbook (U.S. EPA, 1997a). The handbook provides data on drinking water consumption, soil ingestion, inhalation rates, dermal factors including skin area and soil adherence factors, consumption of fruits and vegetables, fish, meats, dairy products, homegrown foods, breast milk, activity patterns, body weight, consumer products, and life expectancy. http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=20563. A set of conditions or assumptions about sources, exposure pathways, amount or concentrations of agent(s)involved, and exposed organism, system or (sub) population (i.e. numbers, characteristics, habits) used to aid in the evaluation and quantification of exposure(s) in a given situation.[26]. Set of conditions or assumptions about sources, exposure pathways, concentrations of toxic chemicals, and populations (numbers, characteristics, and habits) that aid the investigator in evaluating and quantifying exposure in a given situation or set of assumptions concerning how an exposure may take place, including assumptions about the exposure setting, stressor characteristics, and activities that may lead to exposure [11]	
extra risk (ER)	The added risk to that portion of the population that is not included in measurement of background tumor rate.	77
extrapolation , low dose	An estimate of the response at a point below the range of the experimental data, generally through the use of a mathematical model.[1]. 1. In risk assessment, this process entails postulating a biologic reality based on observable responses and developing a mathematical model to describe this reality. The model may then be used to extrapolate to response levels which cannot be directly observed.[13]	80, 125
failure modes and effects analysis	A tool to systematically analyze all contributing component failure modes and identify the resulting effects on the system.	80
false negative results	Results which show no effect when one is there.	80
false positive results	Results which show an effect when one is not there.	80
fate	Pattern of distribution of an agent, its derivatives or metabolites in an organism, system, compartment or (sub) population of concern as a result of transport, partitioning, transformation or degradation [26]. Pattern of distribution of a substance, its derivatives, or metabolites in a system of concern as a result of transport, partitioning, transformation, or degradation [11]. Chemical fate and transport of a pesticide (how it degrades and where it goes) in soil, air, and water. Physical Transport Drift. Describe optimum droplet size and the influence of temperature, humidity, wind speed and direction, volatility and	21, 55

	equipment in altering droplet size and movement. Rainfall and Fog Long-range Transport Chemical Transformation Hydrolysis Oxidation/Reduction Photochemical Reactions Biological Transformation Microbial Bioaccumulation	
Fault tree analysis	A technique by which many events that interact to produce other events can be related using simple logical relationships permitting a methodical building of a structure that represents the system.	80
feasibility study:	Analysis of the practicability of a proposal; e.g., a description and analysis of potential cleanup alternatives for a site such as one on the National Priorities List. The feasibility study usually recommends selection of a cost-effective alternative. It usually starts as soon as the remedial investigation is underway; together, they are commonly referred to as the "RI/FS". A small-scale investigation of a problem to ascertain whether a proposed research approach is likely to provide useful data.	77
food chain	Dependence of a series of organisms, one upon the other, for food. The chain begins with plants and ends with the largest carnivores.	80
fine suspended particulate matter (FSP)	Airborne particles in the range of a diameter smaller than approximately 1 or 2 micrometers	80
fly-ash	Small solid ash particles from the noncombustible portion of fuel that are small enough to escape with the exhaust gases	80
frank effect level (FEL)	Exposure level which produces unmistakable adverse effects, such as irreversible functional impairment or mortality, at a statistically or biologically significant increase in frequency or severity between an exposed population and its appropriate control.	77
Full health	Health state (q.v.) characterized by optimal levels of functioning or capacity in all the important domains health, and freedom from any type of illness or disease. The “optimal” levels of functioning are defined as those levels above which further gains would not (in general) be regarded as improvements in health. States of exceptional functioning above these levels are thus considered to be talents or exceptional abilities, not higher states of health.	27

Functional Residual Capacity (FRC)	The lung volume at the end of tidal expiration (TLC - IC).	125
Term	Definition	Ref.
gamma (multi-hit) model	A generalization of the one-hit dose-response model which provides a better description of dose-response data [8]. A generalization of the one-hit model (see definition) for low-dose extrapolation. The probability P(d) that an individual will respond to lifetime, continuous exposure to dose d is given by $P(d) = \frac{\lambda^k}{\Gamma(k)} \int_0^d t^{k-1} e^{-\lambda t} dt$	77, 125
Gaussian distribution model	A commonly used assumption about the distribution of values for a parameter, also called the normal distribution. For example, a Gaussian a dispersion model is one in which the pollutant is assumed to spread in air according to such a distribution and described by two parameters, the mean and standard deviation of the normal distribution.	77
genetic effect	ffects that are inheritable and appear in the descendants of those exposed.	77
Geographic Informatin System (GIS)	A computer system designed for storing, manipulating, analyzing, and displaying data in a geographic context.	77
Global burden of disease (GBD)	A comprehensive demographic and epidemiological framework to estimate health gaps (q.v.) for an extensive set of disease and injury causes, and for major risk factors, using all available mortality and health data and methods to ensure internal consistency and comparability of estimates. In the first global burden of disease study, Murray and Lopez estimated health gaps using DALYs (q.v.) for eight regions of the world in 1990. This book presents updated estimates for the year 2001 for the world and for World Bank regions.	27
good laboratory practice (GLP)	The formalised process and conditions under which laboratory studies on pesticides are planned, performed, monitored, recorded, reported and audited. Studies performed under GLP are based on the national regulations of a country and are designed to assure the reliability and integrity of the studies and associated data. The US-EPA GLP definition also covers field experiments	36
guidance values (GVs)	Value, such as concentration in air or water, which is derived after allocation of the reference dose among the different possible media (routes) of exposure. The aim of the guidance value is to provide quantitative information from risk assessment to the risk managers to enable them to make	21, 55

	decisions. (See also: reference dose) [26]. value, such as concentration in air or water, that is derived after appropriate allocation of the reference dose among the possible media of exposure to assist regulatory authorities in establishing permissible levels of a potential toxicant [11]	
Guidelines (human health risk assessment):	Guidelines (human health risk assessment): Official, peer-reviewed documentation stating current U.S. EPA methodology in assessing risk of harm from environmental pollutants to populations. Examples: Guidelines for Carcinogenic Risk Assessment: U.S. EPA guidelines intended to guide Agency evaluation of suspect carcinogens. EPA/630/P- 03/001B, 2005. Guidelines for Exposure Assessment: U.S. EPA guidelines intended to guide Agency analysis of potential exposure to chemical substances. 51 FR 22888-22938; May 29,1992. Guidelines for Developmental Toxicity Risk Assessment: U.S. EPA guidelines intended to guide Agency analysis of developmental toxicity data. 51 FR 34028-34040, October 1996. Guidelines for Mutagenicity Risk Assessment: U. S. EPA guidelines intended to guide Agency analysis of mutagenicity data. 51 FR 3400 34016, September, 1986.	125
half-life	The time in which half the atoms of a given quantity of a particular radioactive substance disintegrate to another nuclear form. Measured half-lives vary from millionths of a second to billions of years. Similarly, the time in which half the molecules of a chemical substance disappear as a result of chemical or biochemical transformation.	77
Half-life, biological	The time required for a living organism to eliminate, by natural processes, half the amount of a substance that has entered it.	77
half-life, effective	The time required for a radionuclide contained in a biological system to reduce its activity by half due to the combined result of radioactive decay and biological elimination.	77
hazard	A condition or physical situation with a potential for an undesirable consequence, such as harm to life or limb. [8]. Inherent property of an agent or situation having the potential to cause adverse effects when an organism, system or (sub) population is exposed to that agent [26]. inherent property of an agent or situation capable of having adverse effects on something. Hence, the substance, agent, source of energy, or situation having that property [11]. A hazard, in contrast to risk, refers to the potential that a situation has to cause harm. The hazard is not equivalent to the risk it entails. The hazard is a	21, 55, 77

	characteristic of the stressor that emphasises what could happen if the ecological entity is exposed to the stressor. It does not express how likely it is to happen since that depends on the situation being assessed.	
hazard assessment	An analysis and evaluation of the physical, chemical and biological properties of the hazard [8]. A process designed to determine the possible adverse effects of an agent or situation to which an organism, system or (sub) population could be exposed. The process includes hazard identification and hazard characterization. The process focuses on the hazard in contrast to risk assessment where exposure assessment is a distinct additional step [26]. Process designed to determine factors contributing to the possible adverse effects of a substance to which a human population or an environmental compartment could be exposed. The process includes three steps: hazard identification, hazard characterization, and hazard evaluation . Note: Factors may include mechanisms of toxicity, dose-effect and dose-response relationships, variations in target susceptibility, etc. [11].	21, 55, 77
hazard characterization	The qualitative and, wherever possible, quantitative description of the inherent properties of an agent or situation having the potential to cause adverse effects. This should, where possible, include a dose-response assessment and its attendant uncertainties. Hazard Characterisation is the second stage in the process of Hazard Assessment, and the second step in Risk Assessment. Related terms: Dose-Effect Relationship, Effect Assessment, Dose-Response Relationship, Concentration -Effect Relationship [26]. Tthe second step in the process of hazard assessment, consisting in the qualitative and, wherever possible, quantitative description of the nature of the hazard associated with a biological, chemical, or physical agent, based on one or more elements, such as mechanisms of action involved, biological extrapolation, dose-response and dose-effect relationships, and their respective attendant uncertainties [11]	21, 55
hazard evaluation	A component of risk evaluation that involves gathering and evaluating data on the types of health injury or disease that may be produced by a chemical and on the conditions of exposure under which such health effects are produced [8]. the third step in the process of hazard assessment aiming at the determination of the qualitative and quantitative relationship between exposure to a hazard under certain conditions, including attendant uncertainties and the resultant adverse effect [11]	21, 77

hazard identification	The process of determining whether exposure to an agent can cause an increase in the incidence of a health condition Providing information on which facilities have extremely hazardous substances, what those chemicals are, how much there is at each facility, how the chemicals are stored, and whether they are used at high temperatures [8]. The identification of the type and nature of adverse effects that an agent has as inherent capacity to cause in an organism, system or (sub) population. Hazard identification is the first stage in hazard assessment and the first step in the process of Risk Assessment [26]. the first stage in hazard assessment, consisting of the determination of substances of concern, the adverse effects they may have inherently on target systems under certain conditions of exposure, taking into account toxicity data Note: Definitions may vary in wording, depending on the context. Thus, here: [RISK ASSESSMENT] the first stage in risk assessment, consisting of the determination of particular hazards a given target system may be exposed to, including attendant toxicity data [11] The process of identifying the biological agents that could potentially be introduced in the commodity considered for importation. A hazard represents elements or events that are potentially harmful. In risk assessment, hazard is specified by describing what might go wrong and how this might happen. A particular item or event may not pose a hazard in itself, but its introduction into a scenario where it can cause harm presents a hazard (SPS Agreement).	21, 55, 77
hazard index (HI)	Potential noncarcinogenic (systemic) effects are characterized by comparing projected intakes of chemicals to toxicity values (i.e, reference doses). The numerical risk or hazard quotient estimates that results is a ratio. The ratio of the intake over the reference dose (hazard index) is compared to unity (1.0). If the quotient is less than 1, then the systemic effects are assumed not to be of concern; if the hazard quotient is greater than 1, then the systemic effects are assumed to be of concern. The hazard index is the sum of hazard quotients. Hazard indices (HIS) are calculated by summing hazard quotients for each chemical across all exposure routes. If the HI for any COPC exceeds unity, potential health effects may be a concern from exposure to the COPC. The HI is calculated using the following equation: HI = ···ntakei/Rfdi; Where HI = hazard index (unitless); Intakei= exposure level (intake) for the i" toxicant (mg/kg/day); RfDj = reference dose for the i" toxicant (mg/kg/day); In the foregoing equation, intake and	77

	RfD are expressed in the same units and represent the same exposure time period.	
hazard ranking system (HRS)	The principle screening tool used by EPA to evaluate risks to public health and the environment associated with abandoned or uncontrolled hazardous waste sites. The HRS calculates a score based on the potential of hazardous substances spreading from the site through the air, surface water, or groundwater, and on other factors such as density and proximity of human population. This score is the primary factor in deciding if the site should be on the National Priorities List and, if so, what ranking it should have compared to other sites on the list	77
hazardous air pollutants (HAPs)	Air pollutants which are not covered by ambient air quality standards but which, as defined in the Clean Air Act, may reasonably be expected to cause or contribute to irreversible illness or death. Such pollutants include asbestos, beryllium, mercury, benzene, coke oven emissions, radionuclides, and vinyl chloride.	77
hazardous chemical, hazardous substance:	Any chemical which is a physical hazard or a health hazard as defined under OSHA 29 CFR 1910.1201. An EPA designation for any hazardous material requiring an MSDS under OSHA's Hazard Communication Standard. Such substances are capable of producing fires and explosions or adverse health effects like cancer and dermatitis. Hazardous chemicals are distinct from hazardous waste hazardous substance . Also Hazardous Substance: 1. Any material that poses a threat to human health and- /or the environment. Typical hazardous substances are toxic, corrosive, ignitable, explosive, or chemically reactive. 2. Any substance designated by EPA to be reported if a designated quantity of the substance is spilled in the waters of the United States or if otherwise released into the environment.	77
hazardous waste (HAZ)	HAZ is waste regulated under the Resource Conservation and Recovery Act (RCRA). RCRA regulates solid waste, hazardous waste, and Underground Storage Tanks (USTs) holding petroleum or certain chemicals. Waste that is ignitable, corrosive, reactive, toxic, or contains certain amounts of toxic chemicals is considered hazardous according to the RCRA definition. In Oak Ridge the term Hazardous Waste also included wastes regulated under the Toxic Substances Control Act (TSCA). These are wastes that are contaminated with polychlorobiphenyls (PCB's) or asbestos. When the term Hazardous Waste is used, it implies that the material can be certified NOT to be contaminated with radioactive material, otherwise the term Mixed Waste is used	77
health advisory (HA)	A non-regulatory health-based reference level of chemical traces (usually in ppm) in drinking water at which there are no adverse health risks when ingested over various periods of time. Such	77

	levels are established for one day, 10 days, long term and life-time exposure periods. They contain a large margin of safety. Health Advisory. An estimate of acceptable drinking water levels for a chemical substance based on health effects information; a Health Advisory is not a legally enforceable Federal standard, but serves as technical guidance to assist Federal, State, and local officials. One-Day HA: The concentration of a chemical in drinking water that is not expected to cause any adverse noncarcinogenic effects for up to one day of exposure. The One-Day HA is normally designed to protect a 10-kg child consuming 1 liter of water per day. Ten-Day HA: The concentration of a chemical in drinking water that is not expected to cause any adverse noncarcinogenic effects for up to ten days of exposure. The Ten-Day HA is also normally designed to protect a 10-kg child consuming 1 liter of water per day. Lifetime HA: The concentration of a chemical in drinking water that is not expected to cause any adverse noncarcinogenic effects for a lifetime of exposure. The Lifetime HA is based on exposure of a 70-kg adult consuming 2 liters of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.	
health-adjusted life expectancy (HALE)	Any of a number of summary measures which use explicit weights to combine health expectancies for a set of discrete health states into a single indicator of the expectation of equivalent years of good health. Also referred to as 'Healthy life expectancy'.	27
health Assessment	An evaluation of available data on existing or potential risks to human health posed by a Superfund site. The Agency for Toxic Substances and Disease Registry (ATSDR) of the Department of Health and Human Services (DHHS) is required to perform such an assessment at every site on the National Priorities List	77
health and safety study	Any study of any effect of a chemical substance or mixture on health or the environment or on both, including underlying data and epidemiological studies, studies of occupational exposure to a chemical substance or mixture, toxicological, clinical, and ecological studies of a chemical substance or mixture, and any test performed pursuant to the Toxic Substances Control Act (TSCA)	77
health effect	A deviation in the normal function of the human body.	77
health effect assessment	The component of risk assessment which determines the probability of a health effect given a particular level or range of exposure to a hazard	77
Health expectancy	Generic term for summary measures of population health which	27

(HE)	estimate the expectation of years of life lived in various health states.	
health hazard	1. Acute toxicity: The older term used to describe immediate toxicity. Its former use was associated with toxic effects that were severe (e.g., mortality) in contrast to the term "subacute toxicity" that was associated with toxic effects that were less severe. The term "acute toxicity" is often confused with that of acute exposure. 2. Allergic reaction: Adverse reaction to a chemical resulting from previous sensitization to that chemical or to a structurally similar one. 3. Chronic toxicity: The older term used to describe delayed toxicity. However, the term "chronic toxicity" also refers to effects that persist over a long period of time whether or not they occur immediately or are delayed. The term "chronic toxicity" is often confused with that of chronic exposure. 4. Idiosyncratic reaction: A genetically determined abnormal reactivity to a chemical. 5. Immediate versus delayed toxicity: Immediate effects occur or develop rapidly after a single administration of a substance, while delayed effects are those that occur after the lapse of some time. These effects have also been referred to as acute and chronic, respectively. 6. Reversible versus irreversible toxicity: Reversible toxic effects are those that can be repaired, usually by a specific tissue's ability to regenerate or mend itself after chemical exposure, while irreversible toxic effects are those that cannot be repaired. 7. Local versus systemic toxicity: Local effects refer to those that occur at the site of first contact between the biological system and the toxicant; systemic effects are those that are elicited after absorption and distribution of the toxicant from its entry point to a distant site	77
Healthy life expectancy	Synonym for HALE (q.v.) or Healthadjusted life expectancy.	27
health risk	Risk in which an adverse event affects human health.	77
Health state	Health state (q.v.) characterized by optimal levels functioning or capacity in all the important domains of health, and freedom from any type of illness or disease. The “optimal” levels of functioning are defined as those levels above which further gains would not (in general) be regarded as improvements in health. States of exceptional functioning Health state refers to an individual’s levels of functioning within a set of health domains such as mobility, cognition, pain, emotional functioning, self-care, etc. More specifically, in terms of ICF (q.v.) concepts, health state is defined as the capacities of an individual in all important domains of health, where such domains may include domains of body structure and function, and domains of activities/participation. Health states do not include risk factors, diseases, prognosis or the impact of health states on overall quality of life, well-being or satisfaction.	27

Health status	A general term referring to all aspects of the health of individuals or populations. Usually understood to include mortality risks, diseases, health states (q.v.), impairments and disability. May also include some risk factors or prognosis information.	27
healthy worker effect	The difference in mortality risk due to selection forces between a population of active workers healthy enough to have been (and remain) employed and the general population which includes sick and disabled persons. If working in a safe environment, such a population of active workers has been variously estimated to have a mortality risk 60–90% that of the general population.	77
HEAST	The EPA Superfund Health Effects Assessment Summary Tables (HEAST) database. HEAST contains radionuclide slope factors, RfD, RfC and slope factors for chemical substances.	
Henry's law constant (He)	The Henry's Law constant (H) relates the solubility of a chemical in water (Cw) to the partial pressure of the chemical in the gas phase (P), in the low concentration range in which this relationship is linear. P (Pa) = H (Pa m3 / mol) Cw (mol / m3) The partial pressure can be converted into a concentration in air (Ca) by using the ideal gas law, yielding Ca = H/RT Cw Where R is the ideal gas constant (8.314 Pa m3 / mol K) and T is the absolute temperature (K).	158
high-end exposure estimate (HEEE)	A plausible estimate of individual exposure or dose for those persons at the upper end of an exposure or dose distribution, conceptually above the 90th percentile, but not higher than the individual in the population who has the highest exposure or dose. An estimate of exposure, or dose level received anyone in a defined population that is greater than the 90th percentile of all individuals in that population, but less than the exposure at the highest percentile in that population. A high end risk descriptor is an estimate of the risk level for such individuals. Note that risk is based on a combination of exposure and susceptibility to the stressor. The relationship between answering the questions about high-end individual risk and what the exposure assessor must do to develop the descriptors is discussed in Section 3.4. Individual risk descriptors will generally require the assessor to make estimates of high-end exposure or dose, and sometimes additional estimates (e.g., estimates of central tendency such as average or median exposure or dose).	48
High Risk Community	A community located within the vicinity of numerous sites or facilities or other potential sources of environmental exposure/health hazards which may result in high levels of exposure to contaminants or pollutants. In determining risk or potential risk, factors such as total weight of toxic contaminants, toxicity, routes of exposure, and other factors may be used[8].	77

hockey stick regression function	A dose-response curve that shows zero response up to a presumed physiological threshold value and then a linear increase thereafter.	77
homeostasis	A tendency to stability in the normal body states of the organism.	77
hormesis	is a dose response phenomenon characterized by a low dose stimulation, high dose inhibition, resulting in either a J-shaped or an inverted U-shaped dose response. A pollutant or toxin showing hormesis thus has the opposite effect in small doses than in large doses. As an example, challenging mice with small doses of gamma ray radiation shortly before irradiating them with very high levels of gamma rays actually decreases the likelihood of cancer. There is a similar effect when dioxin is given to rats. The same has long been proposed regarding moderate ambient temperature fluctuations, regular exercise and even limited caloric deprivation, as both immune system stimulants and possible longevity factors. The hormesis model has been shown to hold for numerous other substances and environmental fluctuations. Hormesis, then, is the term for generally-favorable biological responses to low exposures to toxins and other stressors. (Such environmental factors that would seem to produce positive responses have also been termed "eustress".). A very low dose of a chemical agent may trigger from an organism the opposite response to a very high dose. Hormesis is a dose-response phenomenon characterized by low-dose stimulation and high-dose inhibition. Since dose-responses are often believed to be linear from low-dose to high, the non-linear nature of hormesis and its application in all the scientific fields is of rapidly growing interest among scientists and regulators alike. In turn, the International Hormesis Society and its quarterly peer-reviewed journal Dose-Response have been created to promote the understanding of the nature, mechanisms, and implications of the dose-response in general and of hormesis in particular. A clear example of the benefits from understanding hormesis is called alcohol. We know that excessive drinking can rot your liver and kill you. But the evidence appears overwhelming that a little bit of alcohol is good for you, particularly for men over the age of 40. A drink or two at dinner apparently reduces the risk of heart disease and stroke. International Hormesis society: http://www.hormesissociety.org/ http://www.dose-response.com/	168
hot spot	The region in a radiation/ contamination area in which the level of radiation/contamination is significantly greater than in neighboring regions in the area. An area where the concentration of air toxics is significantly higher than background levels, and where exposed individuals may have an elevated risk of adverse health effects.	77

human equivalent concentration (HEC) or dose (HED):	The human concentration (for inhalation exposure) or dose (for other routes of exposure) of an agent that is believed to induce the same magnitude of toxic effect as the experimental animal species concentration or dose. This adjustment may incorporate toxicokinetic information on the particular agent, if available, or use a default procedure, such as assuming that daily oral doses experienced for a lifetime are proportional to body weight raised to the 0.75 power.	12, 125
human exposure evaluation	Describing the nature and size of the population exposed to a substance and the magnitude and duration of their exposure. The evaluation could concern past, current, or anticipated exposures	77
human health risk	The likelihood that a given exposure or series of exposures may have or will damage the health of individuals	77
immediately dangerous to life and health (IDLH)	The maximum level to which a healthy worker can be exposed for 30 minutes and escape without suffering irreversible health effects or escape- impairing symptoms. [6]. The force of impression of one thing on another [8] he current NIOSH definition for an immediately dangerous to life or health condition, as given in the NIOSH Respirator Decision Logic [NIOSH 1987], is a situation "that poses a threat of exposure to airborne contaminants when that exposure is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from such an environment." It is also stated that the purpose of establishing an IDLH is to "ensure that the worker can escape from a given contaminated environment in the event of failure of the respiratory protection equipment." The NIOSH respirator decision logic uses an IDLH as one of several respirator selection criteria. Under the NIOSH respirator decision logic, "highly reliable" respirators (i.e., the most protective respirators) would be selected for emergency situations, fire fighting, exposure to carcinogens, entry into oxygen-deficient atmospheres, entry into atmospheres that contain a substance at a concentration greater than 2,000 times the NIOSH REL or OSHA PEL, and for entry into immediately dangerous to life or health conditions. These "highly reliable" respirators include either a self-contained breathing apparatus (SCBA) that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode, or a supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary SCBA operated in a pressure-demand or other positive-pressure mode.	183
impact	The total, direct and indirect, effects of a programme, service or institution on a health status and overall health and socio-economic impact development [6]. Environmental Impact Assessment can be defined as: The process of identifying, predicting, evaluating and mitigating	77, 183

	the biophysical, social, and other relevant effects of development proposals prior to major decisions being taken and commitments made.	
incidence	The number of new cases of a disease in a population over a period of time [8]. New cases of disease or injury occurring in a specified population in a given time period.[14]	27, 77
incidence rate	New cases of disease or injury occurring per unit of population, per unit time.	27
index chemical	The chemical selected as the basis for standardization of toxicity of components in a mixture. The index chemical must have a clearly defined dose-response relationship.	131
indicator	A variable with characteristics of quality, quantity and time used to measure, directly or indirectly, changes in a situation and to appreciate the progress made in addressing it. It also provides a basis for developing adequate plans for improvement. Variable susceptible of direct measurement that is assumed to be associated with a state that cannot be measured directly. Indicators are sometimes standardized by national or international authorities. Variable that helps to measure changes in a health situation directly or indirectly and to assess the extent to which the objectives and targets of a programme are being attained [6]	183
indicator organisms	A species, whose presence or absence may be characteristic of environmental conditions in a particular area of habitat; however, species composition and relative abundance of individual components of the population or community are usually considered to be a more reliable index of water quality.	77
indirect pathway/indirect exposure	Indirect exposure - Often defined as an exposure involving multimedia transport of agents from source to exposed individual. Examples include exposures to chemicals deposited onto soils from the air, chemicals released into the ground water beneath a hazardous waste site, or consumption of fruits or vegetables with pesticide residues.	48
individual risk	The risk to an individual rather than to a population Individual risk is risk borne by individual persons within a population. Risk assessments almost always deal with more than a single individual. Carcinogenic Risk - The probability, expressed as chances in a million, that a person experiencing 70 years of continuous area-wide outdoor exposure to a toxic air contaminant will develop cancer .	77
individual susceptibility	The marked variability in the manner in which individuals will respond to a given exposure to a toxic agent.	77
intake	The process by which an agent crosses an outer exposure surface of a human or animal without passing an absorption barrier, i.e.	50

	through ingestion or inhalation (see dose).	
Integrated Risk Information System (IRIS)	The Integrated Risk Information System (IRIS) is a database of the U.S. EPA containing human health risk values for over 500 chemicals. The values represent the consensus of the U.S. EPA. IRIS can be accessed online at www.epa.gov/iris. For additional information, contact the U.S. EPA Risk Information Hotline at (301) 345-2870 or at Hotline.IRIS@epamail.epa.gov.	12
inversion	An atmospheric condition caused by a layer of warm air preventing the rise of relatively cool air trapped beneath it. This holds down pollutants that might otherwise be dispersed, and can cause an air pollution episode.	77
in vitro	Outside the living organism. Literally, in glass.	77
in vivo	Within the living organism.	77
ITER (The International Toxicity Estimates for Risk)	(ITER) is a database of international risk values, managed by Toxicology Excellence for Risk Assessment (TERA). ITER provides risk values from health organizations, government agencies and independent groups worldwide in a side-by-side format with a synopsis to explain any differences in values across organi-zations. ITER also provides a link to each organization for more detailed information. ITER is available at http://www.tera.org/iter. ITER contains risk values and/or cancer classifications from 6 organizations: 1. U.S. Agency for Toxic Substances and Disease Registry (ATSDR) 2. Health Canada 3. International Agency for Research on Cancer (IARC) 4. Independent parties (listed under the ITER column) 5. NSF International (NSF Intl) 6. The National Institute of Public Health & Environmental Protection (RIVM) (the Netherlands) and, 7. U.S. Environmental Protection Agency (U.S. EPA) Risk values derived by independent groups will be accepted for inclusion on ITER after undergoing independent peer review and after approval by Toxicology Excellence for Risk Assessment (TERA). We anticipate adding data from the International Programme on Chemical Safety (IPCS), a part of the World Health Organization, in the future.	12
IUCLID	The International Uniform Chemical Information Database: the basic tool for data collection and evaluation in the frame of the European Risk Assessment Programme on Existing Substances. The data structure has been designed to describe the effects of substances on human health and the environment.	31
Term	Definition	Ref.

latency period	period of time from exposure to an agent to the onset of a health effect.	77
leaching	The process by which nutrient chemicals or contaminants are dissolved and carried away by water, or are moved into a lower layer of soil.	77
LED10 (lower effective dose)	The lower confidence limit on an effective dose, that is, in this case the 95% lower confidence limit on a dose associated with 10% response adjusted for background.	176
Level of concern (LOC)	The concentration of an extremely hazardous substance (EHS) in the air above which there may be serious irreversible health effects or death as a result of a single exposure for a relatively short period of time. The concentration in air of an extremely hazardous substance above which there may be serious immediate health effects to anyone exposed to it for short periods. U.S.EPA's Levels of Concern are defined as the concentrations of substances in air above which there may be severe irreversible health effects or death as a result of a single exposure for a relatively short period of time. For most compounds, the level of concern is derived from the existing guidelines listed above (IDLH, TLV, EEGL or ERPG). LOC = 1/10 IDLH	77
lifetime exposure	Total amount of exposure to a substance that a human would receive in a lifetime (usually assumed to be 70 years).	77
line source	Consists of a number of point sources arranged in a straight line, usually across wind (see point source)	77
linear dose response	A pattern of frequency or severity of biological response that varies directly with the amount of dose of an agent. Linear model - A statistical model of a dependent variable y as a function of a factor, x: y = a + bx + E, where E represents random variation.	48, 125
lines of evidence	Information derived from different sources or by different techniques that can be used to describe and interpret risk estimates. Unlike the term "weight of evidence," it does not necessarily imply assignment of quantitative weightings to information.	123
linearized multistage procedure/model	dose-response model based on the multistage model of carcinogenesis that is restricted to a form that is approximately linear at low doses. P(d) = 1 - exp(-q0-q1 x d-...qk x dk) where q1, which is called the linear term, is equal to or greater than zero, d is the average lifetime daily dose of the chemical in mg/kg/day, P(d) is the lifetime probability of cancer from the dose level d, and q0,...,qk are nonnegative parameters estimated by fitting the model to experimental animal carcinogenicity data. The input into this model is the experimental dose, the number of animals with the specific tumor, and the number of animals at risk or examined for that specific tumor. This is often referred to	47

	as quantal data. The quantity of principal interest is not the absolute probability of a cancer P(d), but rather the extra lifetime risk of cancer resulting from exposure to dose d. This risk is defined as [P(d)-P(0)]/[1-P(0)], and can be interpreted as the probability of the occurrence of a tumor at a dose of d, given that no tumor would have occurred in the absence of the dose.	
logistic model	A dose-response model used for low-dose extrapolation, of the form: $P(d) = \gamma + \frac{1-\gamma}{1+e^{-(\alpha+\beta d)}}$ Where: P(d) = probability of cancer from lifetime, continuc α, β = fitted parameters; and γ = background incidence rate.	77, 125
logit model	A dose-response model which, like the probit model, leads to an S-shaped dose-response curve, symmetrical about the 50% response point. The logit model leads to lower "very safe doses" than the probit model even when both models are equally descriptive of the data in the observable range	77
log-probit model	A dose-response model which assumes that each animal has its own threshold dose, below which no response occurs and above which a tumor [or other effect] is produced by exposure to a chemical.	77
long-range transport potential (LRTP)	preliminary selection of priority POPs based on the assessment of potential health effects and on the potential contribution of long-range transport to population exposure and risk.	96
longer-term exposure	Repeated exposure by the oral, dermal, or inhalation route for more than 30 days, up to approximately 10% of the life span in humans (more than 30 days up to approximately 90 days in typically used laboratory animal species).	125
lower (and upper) confidence interval	Confidence Interval (Two-Sided): an estimated interval from the lower to upper confidence limit of an estimate of a parameter. This interval is expected to include the true value of the parameter with a specified confidence percentage, e.g., 95% of such intervals are expected to include the true values of the estimated parameters. Confidence Interval (One-Sided): an interval below the estimated upper confidence limit, or interval above the estimated lower confidence limit, that is expected to include the true value of an estimated parameter with a specified confidence (percent of the time). Confidence Limit: an estimated value below (or above) which the	47

	true value of an estimated parameter is expected to lie for a specified percentage of such estimated limits.	
lower limit on effective dose10 (LED10)	The 95% lower confidence limit of the dose of a chemical needed to produce an adverse effect in 10 percent of those exposed to the chemical, relative to control.	125
lowest-observed-adverse effect level (LOAEL)	The lowest dose in an experiment which produced an observable adverse effect.	77
lowest observed effect level (LOEL)	The Lowest-Observed-Effect-Level (LOEL) is the lowest exposure level at which there are statistically or biologically significant increases in frequency or severity of an effect between the exposed population and its appropriate control group.	12
Mackay models	Models which attempt to predict the environmental compartment into which the chemical will partition and the equilibrium concentration can also provide important insights for the environmental hazards of chemicals. Some of these models are available on the Internet at http://www.trentu.ca/academic/aminss/envmodel/welcome.html . ChemCAN (Mackay level III model) Model used Health Canada. It estimates average concentrations in air, fresh surface water, fish, sediments, soils, vegetation, and marine near-shore waters. It is intended to assist in human exposure assessment. Designed for use in Canada, a database of 24 regions of Canada is included. Other regions can be defined by the user and added to the database, however, areas should have a radius of at least 300 km (http://www.trentu.ca/cemc/models/CC600.html)	59
margin of exposure (MOE)	Ratio of the no-observed-adverse-effect level (NOAEL) for the critical effect to the theoretical, predicted or estimated exposure dose or concentration. Related term: Margin of Safety [26]. Rratio of the no-observed-adverse- effect level (NOAEL) to the estimated exposure dose (EED) or concentration (EEC) Note: In the case of environmental risk assessment, predicted environmental concentration (PEC) is used instead of EEC [11]. The point of departure divided by a human environmental exposure(s) of interest, actual or hypothetical [42] . The ratio of the point of departure (POD) over an exposure estimate (MOE = POD/Exposure)[44]. In the risk characterization process, a comparison is made between the RfD and the estimated (calculated or measured) exposure dose (EED). The EED should include all sources and routes of exposure involved. If the EED is less than the RfD, the need for regulatory concern is likely to be small. An alternative measure that may be useful to some risk managers is the margin of exposure (MOE), which is the magnitude by which	21, 55, 118

	the NOAEL of the critical toxic effect exceeds the estimated exposure dose (EED), where both are expressed in the same units: MOE = NOAEL (experimental dose) / EED (human dose). When the MOE is equal to or greater than UF x MF, the need for regulatory concern is likely to be small.	
margin of safety (MOS)	For some experts the Margin of Safety has the same meaning as the Margin of Exposure, while for others, the Margin of Safety means the margin between the reference dose and the actual exposure dose or concentration. Related term: Margin of Exposure [26]	47, 55
mass median aerodynamic diameter (MMAD)	The diameter that divides the mass distribution of an aerosol in half.	77
Maximum acceptable toxic concentration (MATC)	For a particular ecological effects test, this term is used to mean either the range between the NOAEL and the LOAEL or the geometric mean of the NOAEL and the LOAEL. The geometric mean is also known as the chronic value.	124
maximum contaminant level (MCL)	The maximum permissible level of a contaminant in water delivered to any user of a public system. MCLs are enforceable standards. Maximum Contaminant Level. The highest level of a contaminant that is allowed in drinking water. MCLs are set as close to the MCLG as feasible using the best available analytical and treatment technologies and taking cost into consideration. MCLs are enforceable standards.	77
maximum contaminant level goal (MCLG)	Under the Safe Drinking Water Act, a non-enforceable concentration of a drinking water contaminant, set at the level at which no known or anticipated adverse effects on human health occur and which allows an adequate safety margin. The MCLG is usually the starting point for determining the regulated Maximum Contaminant Level. Maximum Contaminant Level Goal. A non-enforceable health goal which is set at a level at which no known or anticipated adverse effect on the health of persons occurs and which allows an adequate margin of safety.	77
maximum likelihood estimate (MLE), maximum Likelihood (ML) method	Statistical method for estimating a population parameter most likely to have produced the sample observations.	125
maximum permissible risk	is the general term used by RIVM to indicate the limit value(s), including TDI, TCA, CR(oral), and CR(inhal).	12

(MPR)		
maximum tolerated dose (MTD)	The maximum doses that an animal species can tolerate for a major portion of its lifetime without significant impairment or toxic effect other than carcinogenicity maximum tolerable dose (MTD): Highest amount of a substance that, when introduced into the body, does not kill test animals (denoted by LDo)	77
measurement endpoint	Measurable (ecological) characteristic that is related to the valued characteristic chosen as an assessment point.	55
measures of central tendency	A general term for several characteristics of the distribution of a set of values or measurements around a value or values at or near the middle of the set. The principal measures of central tendency are the mean (average), median, and mode.	48
measure of ecosystem and receptor characteristics	Measures that influence the behavior and location of ecological entities of the assessment endpoint, the distribution of a stressor, and lifehistory characteristics of the assessment endpoint or its surrogate that may affect exposure or response to the stressor.	124
measure of effect	A change in an attribute of an assessment endpoint or its surrogate in response to a stressor to which it is exposed.	124
Measure of exposure	A measure of stressor existence and movement in the environment and its contact or co-occurrence with the assessment endpoint.	124
media / medium	Material (e.g., air, water, soil, food, consumer products) surrounding or containing an agent.	50
medium intake rate	The rate at which the medium crosses the outer exposure surface of an animal or human.	50
microenvironment	Surroundings that can be treated as homogeneous or well characterized in the concentrations of an agent (e.g., home, office, automobile, kitchen, store) [49]. Microenvironment method - A method used in predictive exposure assessments to estimate exposures by sequentially assessing exposure for a series of areas (microenvironments) that can be approximated by constant or well-characterized concentrations of a chemical or other agent. A method for sequentially assessing exposure for a series of microenvironments that can be approximated by constant concentrations of a stressor. Well-defined surroundings such as the home, office, automobile, kitchen, store, etc. that can be treated as homogeneous (or well characterized) in the concentrations of a chemical or other agent.	48, 50
minimal risk level (MRL)	An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. MRLs are based on noncancer health effects only and	12

	are not based on a consideration of cancer effects. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean-up or action levels. MRLs are derived for hazardous substances using the no-observed-adverse-effect level/uncertainty factor approach. They are below levels that might cause adverse health effects in the people most sensitive to such chemical-induced effects. MRLs are derived for acute (1-14 days), intermediate (15-364 days), and chronic (365 days and longer) durations and for the oral and inhalation routes of exposure. Used by ATSDR (http://www.atsdr.cdc.gov/mrls.html).	
mobile source	A moving producer of air pollution, mainly forms of transportation - cars, motorcycles, planes.	77
mobility	The ability of a chemical element or a pollutant to move into and through the environment (e.g., the mobilization of an element from a water column to sediment).	77
monitoring	Periodic or continuous surveillance or testing to determine the level of compliance with statutory requirements and/or pollutant levels in various media or in humans, plants, and animals.	77
Monte Carlo Analysis	One of several mathematical techniques for performing proba-bilistic assessments. The method relies on the computational powers of modern computers to simulate the range and frequency of all possible outcomes of a process based on repeatedly sampling from the inputs provided by the user. These inputs are combined according to the model that is specified by the user.	118
morbidity	departure from a state of physical or mental well-being, resulting from disease or injury. Frequently used only if the affected individual is aware of the condition. Awareness itself connotes a degree of measurable impact. Frequently, but not always, there is a further restriction that some action has been taken such as restriction of activity, loss of work, seeking of medical advice, etc	77
mortality (rate)	Death; the death rate; ratio of number of deaths to a given population. The number of deaths that occur in a given population during a given time interval; usually deaths per 103 or 105 people per year. Can be age, sex, race, and cause specific.	77
multimedia approach (exposure)	Multimedia exposure - Exposure to a toxic substance from multiple pathways such as air, water, soil, food, and breast milk. A process for considering several environmental media, such as air, water, and land, together, rather than in isolation.	48
multistage model	A carcinogenesis dose-response model where it is assumed that cancer originates as a "malignant" cell, which is initiated by a series of somatic-like mutations occurring in finite steps. It is also assumed that each mutational stage can be depicted as a Poisson	77, 125

	process in which the transition rate is approximately linear in dose rate [8]. A mathematical function used to extrapolate the probability of cancer from animal bioassay data, using the form: $P(d) = 1 - e^{-(q_0 + q_1 d + q_2 d^2 + \ldots + q_k d^k)}$ Where: P(d) = probability of cancer from a continuous, lifetime exp q_i = fitted dose coefficients of model; i=0, 1, . . ., k; and k = number of stages selected through best fit of the mode than one less than the number of available dose groups.	
multistage Weibull model:	A dose-response model for low-dose extrapolation that includes a term for decreased survival time associated with tumor incidence: $P(d,t) = 1 - e^{-(q_0 + q_1 d + q_2 d^2 + \ldots + q_k d^k)(t - t_0)^z}$ Where: P(d,t) = the probability of a tumor (or other response) from continuous exposure at dose d until age t (when tumor is f q_i = fitted dose parameters, i=0, 1, . . ., k; k = no greater than the number of dose groups - 1; t_0 = the time between when a potentially fatal tumor becom and when it causes death; and z = fitted time parameter (also called "Weibull" parameter)	125
mutagen	A substance that can induce alterations in the DNA of either somatic or germinal cells.	77, 125
Term	Definition	Ref.
National Emissions Standards for Hazardous Air Pollutants (NESHAPS)	Emissions standards set by EPA for an air pollutant not covered by NAAQS that may cause an increase in fatalities or in serious, irreversible, or incapacitating illness. Primary standards are designed to protect human health, secondary standards to protect public welfare (e.g., building facades, visibility, crops, and domestic animals).	77
National Proirities List (NPL)	EPA's list of the most serious uncontrolled or abandoned hazardous waste sites identified for possible long-term remedial action under Superfund. The list is based primarily on the score a site receives from the Hazard Ranking System. EPA is required to update the NPL at least once a year. A site must be on the NPL to	77

	receive money from the Trust Fund for remedial action	
noncancer toxicity	Local and systemic effects caused by chemical exposures that are not cancer. These effects are generally considered to have a threshold in response.	12
non-linear dose response	A pattern of frequency or severity of biological response that does not vary directly with the amount of dose of an agent [1]. relationship that cannot be expressed simply as the change in response being proportional to the amount of change of some function of dose [76].	47, 125
nonpoint-source pollution	A contributing factor to water pollution that cannot be traced to a specific spot; like agricultural fertilizer runoff, sediment from construction.	77
no-observed-adverse-effect level (NOAEL)	From long-term toxicological studies of agriculture chemical active ingredients, levels at which indicate a safe, lifetime exposure level for a given chemical. Used to establish tolerance for human diets. Also written, NOEL[8]. The highest exposure level at which there are no biologically significant increases in the frequency or severity of adverse effect between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered adverse or precursors of adverse effects [1]	77, 125
no-observed-effect level (NOEL)	An exposure level at which there are no statistically or biologically significant increases in the frequency or severity of any effect between the exposed population and its appropriate control [1]. The No-Observed-Effect Level (NOEL) is an exposure level at which there are no statistically or biologically significant increases in the frequency or severity of any effect between the exposed population and its appropriate control [14]	12, 125
NSF International	an independent, not-for-profit organization, prepares compound specific oral risk assessment documents based on the requirements of Annex A of NSF International/American National Standards 60 "Drinking water treatment chemicals - Health effects" and 61 "Drinking water system components - Health effects". Oral RfDs or cancer risk levels are derived using U.S. EPA risk assessment guidelines. NSF/ANSI standards and oral risk assessment documents prepared by NSF are available on-line at the NSF Bookstore. NSF/ANSI Standards 60 or 61, which include Annex A, are available at: http://www.techstreet.com/cgi-bin/browsePublisher?publisher_id=133&orderBy=doc_no. Compound specific oral risk assessment documents prepared by NSF International are available at: http://www.techstreet.com/cgi-bin/browsePublisher?publisher_id=133&subgroup_id=13180.	12
octanol/water partition coefficient (Kow	The octanol/water partition coefficient. This coefficient is unitless.	31

or P)		
Odds Ratio (OR)	A relative measure of the difference in exposure between the diseased (cases) and not diseased (controls) individuals in a case-control study. The OR is interpreted similarly to the relative risk. t is defined as the ratio of the odds of an event occurring in one group to the odds of it occurring in another group, or to a sample-based estimate of that ratio. These groups might be men and women, an experimental group and a control group, or any other dichotomous classification. If the probabilities of the event in each of the groups are p (first group) and q (second group), then the odds ratio is: $$\frac{p/(1-p)}{q/(1-q)} = \frac{p(1-q)}{q(1-p)}.$$ An odds ratio of 1 indicates that the condition or event under study is equally likely in both groups. An odds ratio greater than 1 indicates that the condition or event is more likely in the first group. And an odds ratio less than 1 indicates that the condition or event is less likely in the first group. The odds ratio must be zero or greater than zero. As the odds of the first group approaches zero, the odds ratio approaches zero. As the odds of the second group approaches zero, the odds ratio approaches positive infinity. For example, suppose that in a sample of 100 men, 90 have drunk beer in the previous week, while in a sample of 100 women only 20 have drunk beer in the same period. The odds of a man drinking beer are 90 to 10, or 9:1, while the odds of a woman drinking beer are only 20 to 80, or 1:4 = 0.25:1. Now, 9/0.25 = 36, so the odds ratio is 36, showing that men are much more likely to drink beer than women. Using the above formula for the calculation yields: $$\frac{0.9/0.1}{0.2/0.8} = \frac{0.9 \times 0.8}{0.1 \times 0.2} = \frac{0.72}{0.02} = 36.$$ This example also shows how odds ratios can sometimes seem to overstate relative positions: in this sample men are 4.5 times more likely to have drunk beer than women, but have 36 times the odds. Taking the logarithm of the odds ratio ameliorates this effect, and also improves symmetry. For example, using natural logarithms, an odds ratio of 36 maps to 3.584, an odds ratio of one maps to zero, and an odds ratio of 1/36 maps to -3.584. The logarithm of the odds-ratio is the difference of the logits of the probabilities. The increased use of logistic regression in medical and social	125

	science research means that the odds ratio is commonly used as a means of expressing the results in some forms of clinical trials, such as case-controlled trials, and in survey research. It is often abbreviated "OR" in reports. When data from multiple surveys is combined, it will often be expressed as "Pooled OR".	
Oncogene, Oncogenic	A substance that causes tumors, whether benign or malignant.	77
one-hit model	The basic dose-response model based on the concept that a tumor can be induced by a single receptor that has been exposed to a single quantum or effective dose unit of a chemical [8]. A dose-response model based on a mechanistic argument that there is a response after a target site has been hit by a single biologically effective unit of dose within a given time period. The form of the model, a special case of the gamma, multistage, and Weibull models, is given by: $P(d) = 1 - e^{(-\lambda d)}$ Where P(d) = probability of cancer from lifetime continuous expo λ = fitted dose coefficient.	77, 125
organic carbon partition coefficient (Koc)	The partition coefficient between organic carbon and water, in units of l/kg.	31
organoleptic	Affecting or involving a sense organ such as that of taste, smell, or sight.	125
OSHA (Occupational Safety and Health Administration)	Occupational Safety and Heath Administration of the U.S. Department of Labor. Federal agency with safety and health regulatory and enforcement authorities for most U.S. industry and business.	77
particle	A tiny mass of material. Airborne particles, materials that exist in the atmosphere as a solid or liquid, can be natural, caused by stirring of soil dusts, or anthropogenic. They vary in size from coarse (diameter > 3 µm) to fine (< 3µm) . Sometimes inhalable or respirable is used to describe those particles (< 2 µm) which can be inhaled through the nose and enter the lungs.	77
partition coefficient for adsorption of the chemical onto a specific substance (Kd)	Partition coefficient for adsorption of the chemical onto a specific substance - i. e. sewage sludge or soil. Obtained from experi-mental measurements by dividing the concentration of chemical adsorbed, in units of mg chemical per kg solid, by the concen-tration remaining in solution, in units of mg/l, to give a partition constant withunits of l/kg.	31

pathway of exposure	The physical course a pesticide takes from the source to the organism exposed (e.g., through food or drinking water consumption or residential pesticide uses).	118, 149
persistence	Persistence generally refers to environmental persistence: the length of time a chemical stays in the environment, once introduced. Persistent chemicals do not break down easily in the environment. The quality of remaining for a long period of time (such as in the environment or the body). Persistent chemicals (such as DDT and PCBs) are not easily broken down. Refers to the length of time a compound stays in the environment, once introduced. A compound may persist for less than a second or indefinitely.	48
persistence and long-range transport of organic chemicals	The long-range transport of air pollution has been recognized as an important factor affecting ecosystems and human populations. The UNECE Convention on Long-range Transboundary Air Pollution is a powerful international instrument that aims to reduce and prevent air pollution. The effects of the Convention can be assessed by the reduction in emissions of pollution by the countries that are Parties to the Convention. However, an impor- tant criterion of the effectiveness of the Convention is its ability to prevent or reduce the burden of long-range air pollution on the environment and human health. the risk assessment would be conducted: pentachlorophenol, DDT, hexachlorocyclohexanes, hexachlorobenzene, heptachlor, polychlorinated dibenzo-p-dioxins and dibenzofurans, polychlorinated biphenyls and polycyclic aromatic hydrocarbons (UNECE, 2000). In addition, a short hazard assessment was planned for polychlorinated, terphenyls, polybrominated diphenylethers, polybrominated dibenzo-pdioxins and dibenzofurans, short-chain chlorinated paraffins and ugilec.	96
persistent organic pollutants (POPs)	Persistent organic pollutants" (POPs) are organic substances that: (i) possess toxic characteristics; (ii) are persistent; (iii) bioaccumulate; (iv) are prone to long-range transboundary atmospheric transport and deposition; and (v) are likely to cause significant adverse human health or environmental effects near to and distant from their sources. The chemicals known as persistent organic pollutants act as powerful pesticides and serve a range of industrial purposes. Some POPs are also released as unintended by-products of combustion and industrial processes.While the risk level varies from POP to POP, by definition all of these chemicals share four properties: 1) They are highly toxic; 2) they are persistent, lasting for years or even decades before degrading into less dangerous forms; 3) they evaporate and travel long distances through the air and through water; and 4) they accumulate in fatty tissue. Persistent organic pollutants (POPs) are organic compounds of	69, 95, 96, 169

	anthropogenic origin that resist degradation and accumulate in the food-chain. They can be transported over long distances in the atmosphere, resulting in widespread distribution across the earth, including regions where they have never been used. Owing to their toxicity, they can pose a threat to humans and the environment. The Protocol on POPs to the UNECE Convention on Long-range Transboundary Air Pollution addresses several of those compounds, namely Aldrin (CAS: 309-00-2), Chlordane (57-74-9), Chlordecone , DDT, Dieldrin, Endrin , Heptachlor , Hexabromobiphenyl, Hexachlorobenzene, Mirex , Toxaphene , hexachlorocyclohexanes, polyaromatic hydrocarbons (benzo(a)pyrene, benzo(b)fluoranthene, benzo(k)fluoranthene, and indeno(1,2,3-cd)pyrene), polychlorinated biphenyls, polychlorinated dibenzodioxins and dibenzofurans [61], Cadmium , Lead , Mercury [62,63], nitrogen oxides, sulfur emissions, particulate matter [64].	
physiologically based pharmacokinetic (PBPK) model	A model that estimates the dose to a target tissue or organ by taking into account the rate of absorption into the body, distribution among target organs and tissues, metabolism, and excretion.	125
pica	Deliberate ingestion of non-nutritive substances such as soil. once introduced.[49] Deliberate ingestion of non-nutritive substances such as soil [55].	48, 50
plume	· The cloud of steam or smoke that comes from a chimney stack and blows downwind. · The contaminated portion of groundwater that moves past a source of pollution.	77
point source	A single isolated stationary source of pollution.	77
point of departure	The dose-response point that marks the beginning of a low-dose extrapolation. This point can be the lower bound on dose for an estimated incidence or a change in response level from a dose-response model (BMD), or a NOAEL or LOAEL for an observed incidence, or change in level of response [1]. Point on the dose-response curve where each chemical's response is close to or within the background level of response, in other words, the dose at which effects are first distinguishable. Depending on the kind of data available and the purpose of the analysis, there are differing procedures for estimating the point of departure [42].	118, 125
point-of-contact approach / point-of-contact measurement of exposure	An approach to quantifying exposure by taking measurements of concentration over time at or near the point of contact between the chemical and an organism while the exposure is taking place [44]. An approach to quantifying exposure by taking measurements of concentration over time at or near the point of contact between the chemical and an organism while the	48

	exposure is taking place. Estimating exposure by measuring concentrations over time (while the exposure is taking place) at or near the place where it is occurring [55]	
pollutant	Any material entering the environment that has undesired effects.	77
pollution	The presence of matter or energy whose nature, location or quantity produces undesired environmental effects.	77
population at risk	A limited population that may be unique for a specific dose-effect relationship; the uniqueness may be with respect to susceptibility to the effect or with respect to the dose or exposure itself.	77
population attributable fraction (PAF)	Proportional reduction in disease or injury that would occur if population exposure to a risk factor or group of risk factors were reduced to an alternative distribution. Occurrence of a disease or death among two population groups, such as those exposed to a risk factor and those not exposed.	27
potential dermal exposure	The total amount of pesticide coming into contact with the protective clothing, work clothing and exposed skin.	48
potentiation	When one substance does not have a toxic effect on a certain organ or system, but when added to a toxic chemical, it makes the latter more toxic.	131
ppb	A unit of measure expressed as parts per billion. Equivalent to 1 x 10-9.	125
ppm	Parts per million. A unit of measure expressed as parts per million. Equivalent to 1 x 10-6. A measurement of concentration such as 1 µg per gram. To convert from ppm to mg/m3. mg/m3 = (ppm) x (molecular weight of the substance)/(24.45). For example, formaldehyde: 1.23 mg/m3 = (1 ppm) x (30.03)/(24.45).	77, 125
precautionary principle	The precautionary principle is a reasonable, rational, and responsible approach to decision-making. It provides a framework for policy making that promotes human health, a sustainable environment, and ensures that future generations of all species have an opportunity to thrive. When an activity raises threats of harm to human health or the environment, precautionary measures should be take even if some cause and effect relationships are not fully established scientifically. · proportional to the chosen level of protection, · non-discriminatory in their application, · consistent with similar measures already taken, · based on an examination of the potential benefits and costs of action or lack of action (including, where appropriate and feasible, an economic cost/benefit analysis), · subject to review, in the light of new scientific data, and	23, 90

	· capable of assigning responsibility for producing the scientific evidence necessary for a more comprehensive risk assessment.	
precision	A measure of how consistently the result is determined by repeated determinations without reference to any "true" value. The closeness of agreement between the results obtained by applying the experimental procedure several times under prescribed conditions (ISO, 1977). Measure for the reproducibility of measurements within a set, that is of the scatter or dispersion of a set about its central value [)ECD, 1996]..	77
predicted environmental concentration (PEC)	The calculated concentration of a substance where no harmful effects to the environment are expected. PNEC is derived from all available test results for a substance. When the extent of available data is limited, safety factors are utilised to take the uncertainty in the data/information into consideration.	31
predicted no effect concentration (PNEC)	The calculated concentration of a substance where no harmful effects to the environment are expected. PNEC is derived from all available test results for a substance. When the extent of available data is limited, safety factors are utilised to take the uncertainty in the data/information into consideration.	31
prevalence	Actual number of cases of disease or injury present in a popu-lation at any particular moment in time [12]. The proportion of disease cases that exist within a population at a specific point in time, relative to the number of individuals within that population at the same point in time [1]	27, 125
prevention	is defined as the promotion of health by the individual and the community, and includes identifying departures from good health and intervening to correct them or to minimize their effects. Primary poisons prevention activities intervene before the event, aiming to prevent it happening, either by controlling the victim's access to the agent, controlling the action of an agent upon the victim, or controlling or changing hostile environmental factors. Primary prevention strategies may be active or passive. · Active strategies seek to change attitudes, lifestyles and behaviours of individuals and groups, for example, by educating communities and individuals about poison awareness and safety practices, or campaigning for initiatives such as safer packaging, labelling and storage of chemical products. · Passive strategies automatically protect people, by improving the safety of products and the environment where they are used. Once these changes are made, they require little individual effort from the beneficiary and can have a far-reaching impact. Secondary poisons prevention is the action taken after an exposure has occurred, to prevent the poisoning from progressing to a more serious, irreversible or chronic stage and to	33

	restore the victim to his/her former state of health. It includes the initial steps to minimize the effects of the toxic agent, the diagnosis, decontamination and first aid treatment, and specific antidote therapy.1 This may include educating both the community and professionals about how to recognize and manage poisonings and how to give first aid after a toxic exposure by, for example, washing the skin and eyes immediately after contamination by a pesticide. Tertiary poisons prevention deals with the diagnosis and treatment of poisoning victims who cannot be treated to full recovery, to prevent death or permanent disability. It is also concerned with educating victims and their relatives about how to make the most of the remaining potential for healthy living, including the avoidance of unnecessary hardships, restrictions and complications, i.e., rehabilitation and physiotherapy in cases of toxic polyneuropathy.	
probabilistic approaches/analysis	Calculation and expression of health risks using multiple risk descriptors to provide the likelihood of various risk levels. Probabilistic risk results approximate a full range of possible outcomes and the likelihood of each, which often is presented as a frequency distribution graph, thus allowing uncertainty or variability to be expressed quantitatively	48
probabilistic uncertainty analysis	Technique that assigns a probability density function to each input parameter, then randomly selects values from each of the distributions and inserts them into the exposure equation. Repeated calculations produce a distribution of predicted values reflecting the combined impact of variability in each input to the calculation. Monte Carlo is a common type of probabilistic uncertainty analysis	48
probability	A probability assignment is a numerical encoding of the relative state of knowledge [8]. The degree to which there is a likelihood that adverse effects will occur from a pest or a disease. The evidence of existing or potential presence of a pest or disease and the likelihood of adverse effects is a key factor influencing the analysis of probability. It also is a factor that influences the degree of confidence regarding the evidence. Evidence is: 1).Data collected as part of a risk; assessment investigation; 2).The quantity or quality of the data that is collected (SPS Agreement).	48, 77
probability of death	The chance that an individual, alive at age x, will be dead before his or her (x _ n)th birthday, usually written as nqx . 5q0 denotes the probability that a newborn infant will die before his or her fifth birthday.	27
probable error	The magnitude of error which is estimated to have been made in determination of results.	77
probit analysis	A statistical transformation which will make the cumulative	77

	normal distribution linear. In analysis of dose-response, when the data on response rate as a function of dose are given as probits, the linear regression line of these data yields the best estimate of the dose-response curve. The probit unit is y = 5 + Z(p) , where p = the prevalence of response at each dose level and Z(p) = the corresponding value of the standard cumulative normal distribution	
probit model	A dose-response model of the form: $P(d) = \gamma + (1-\gamma)\frac{1}{\sqrt{2\pi}}\int_{-\infty}^{\alpha+\beta d} e^{-\frac{u^2}{2}} du$ Where: P(d) = the probability that an individual selected at rando a normal distribution of tolerances; α, β = fitted parameters; and γ = background response rate.	125
problem formulation	A phase of integrated risk assessment that evaluates characteristics of the stressor(s), human/ecological system, and receptors, identifies assessment endpoints, develops one or more conceptual models, and develops an analysis plan.	116
promoter(s)	An agent that is not carcinogenic itself, but when administered after an initiator of carcinogenesis, stimulates the clonal expansion of the initiated cell to produce a neoplasm.	125
proportionate mortality ratio (PMR)	The fraction of all deaths from a given cause in the study population divided by the same fraction from a standard population. A tool for investigating cause-specific risks when only data on deaths are available. If data on the population at risk are also available, SMRs are preferred [8]. The proportion of deaths due to the disease of interest in the exposed population divided by the proportion of deaths due to the disease of interest in the unexposed or reference population. It is frequently converted to a percent by multiplying the ratio by 100 [1]	77, 125
prospective study	An inquiry in which groups of individuals are selected in terms of whether they are or are not exposed to certain factors, and then followed over time to determine differences in the rate at which disease develops in relation to exposure to the factor. Also see cohort study. Prospective studies, also called cohort studies, select subjects based on their exposure status, and subjects are generally healthy at the beginning of the study. The cohort is followed through time to assess their later disease or outcome status. An example of a cohort study would be watching a group of smokers versus nonsmokers through time and measuring incidence of eventual lung cancer. The same 2x2 table is constructed as with the case control study. However, the statistic	77

	generated is the Relative Risk (RR), which is the incidence of disease in the exposured group (A/A+B) over the incidence in the unexposed (C/C+D). As with the OR, a RR greater than 1 shows association, where the conclusion can be read "those with the exposure were more likely to develop disease." Prospective studies have many benefits over case control studies. The RR is a more powerful statistic than the OR, as the OR is just an estimation of the RR, since true incidence cannot be calculated in a case control study where subjects are selected based on disease status. Temporality can be established in a prospective study, and confounders are more easily controlled for. However, they are more costly, and there is a greater chance of losing subjects to follow-up based on the long time period over which the cohort is followed.	
quality of life	is an important concern in economics and political science. There are many components to well-being. A large part is standard of living, the amount of money and access to goods and services that a person has; these numbers are fairly easily measured. Others like freedom, happiness, art, environmental health, and innovation are far harder to measure and could be more important. This has created an inevitable imbalance as programs and policies are created to fit the easily available economic numbers while ignoring the other measures, that are very difficult to plan for or assess. Debate on quality of life is millennia-old, with Aristotle giving it much thought in his Nicomachean Ethics and eventually settling on the notion of eudaimonia, a Greek term often translated as happiness, as central. The neologism liveability (or livability), from the adjective liv(e)able, is an abstract noun now often applied to the built environment or a town or city, meaning its overall contribution to the quality of life of inhabitants. Understanding quality of life is today particularly important in health care, where monetary measures do not readily apply. Decisions on what research or treatments to invest the most in are closely related to their effect of a patient's quality of life. WHO defines Quality of Life as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment. Quality of life must be considered in the context of local development and human needs. It is a subjective evaluation of the situation of a person or group of people and is affected by a range of factors such as those determining health and happiness (including comfort in the physical environment and a satisfactory occupation); education;	168, 173

	social and intellectual fulfilment; freedom of action; justice; and freedom from oppression. This concept is the composite measure of physical, mental and social well-being as perceived by each individual or group of individuals [35]	
Quality-adjusted life years (QALYs)	a measure of the benefit of a medical intervention. It is based on the number of years of life that would be added by the intervention. Each year in perfect health is assigned the value of 1.0 down to a value of 0 for death. If the extra years would not be lived in full health, for example if the patient would lose a limb, or be blind or be confined to a wheelchair, then the extra life-years are given a value between 0 and 1 to account for this. QALYs are controversial as the measurement is used to calculate the allocation of healthcare resources based upon a ratio of cost per QALY. As a result some people will not receive treatment as it is calculated that the benefit to their quality of life is not warranted by the cost.[9]. A measure of years of life lived (or gained through an intervention) adjusted for quality of life using health state preferences rangi between 0 (states equivalent to death) through to 1 (full health). QALYs were developed for the assessment of the cost-effectiveness interventions in health economics. QALYs gained and DALYs averted through an intervention are calculated in very similar ways, and the main differences relate to the interpretation of the weights. Whereas the disability weights in the DALY quantify loss of health, the corresponding QALY weights are often interpreted in terms of well-being, quality of life, or utility.[14]	27, 168
quantal dose-response relationship	dichotomous (Binomial) classification where an individual or animal is placed in one of two categories, e.g., dead or alive, with or without a particular type of tumour, normal or abnormal level of a hormone.	47
quantitative structure activity relationships (QSARs)	are based on a comparison of the structure or some physico-chemical property of a substance ("descriptor") with a measured endpoint which may be another physico-chemical property or a biological effect. QSARs are normally taken to mean a mathematical relationship between a descriptor and a biological or physico-chemical endpoint.	158
PM10	Particulate matter in air less than 10 µm in diameter. Currently used as the measure of exposure for potential effects on human health of particulate matter	77
Term	Definition	Ref.
random error	Indefiniteness of result due to finite precision of experiment. Measure of fluctuation in result upon repeated experimentation.	77, 48
random samples	A sample that is arrived at by selecting sample units such that each possible unit has a fixed and determinate probability of	48

	selection. A sample selected from a statistical population such that each individual has an equal probability of being selected	
range	The difference between the largest and smallest values in a measurement data set.	48
receptor	The ecological entity exposed to the stressor.	124
reasonable maximum exposure (RME)	Used in conservative exposure assessment calculations; based not on worst-case scenario, but on 90% or 95% upper confidence limits on input parameters.	48
reasonable worst case	Reasonable unfavorable but not unrealistic situation: covering normal use patterns, including cases where populations are exposed to the same substance in more than one scenario, e.g. consumers or workers may use several products containing the same substance. The reasonable worst case prediction should also consider upper estimates of the extreme use and reasonably foreseeable misuse. The lower portion of the "high end" of the exposure, dose, or risk distribution. The reasonable worst case conceptually should be targeted at or above the 90th percentile in the distribution, but below the 98th percentile. A semiquantitative term referring to the lower portion of the high end of the exposure, dose, or risk distribution. The reasonable worst case has historically been loosely defined, including synonymously with maximum exposure or worst case, and assessors are cautioned to look for contextual definitions when encountering this term in the literature. As a semiquantitative term, it is sometimes useful to refer to individual exposures, doses, or risks that, while in the high end of the distribution, are not in the extreme tail. For consistency, it should refer to a range that can conceptually be described as above the 90th percentile in the distribution, but below about the 98th percentile. (compare maximum exposure range, worst case). An estimate of the individual dose, exposure, or risk level received by an individual in a defined population that is greater than the 90th percentile but less than that received by anyone in the 98th percentile in the same population.	48
receptor population	The exposed individual relative to the exposure pathway considered.	48
recommended exposure limits (REL)	An 8_ or 10_hour time_weighted average (TWA) or ceiling (C) exposure concentration recommended by NIOSH that is based on an evaluation of the health effects data.	48
recommended maximum contaminant level (RMCL)	The maximum level of a contaminant in drinking water at which no known or anticipated adverse affect on human health would occur, and that includes an adequate margin of safety. Recommended levels are nonenforceable health goals	77
reconstruction of dose	An approach to quantifying exposure from internal dose, which is in turn reconstructed after exposure has occurred, from evidence	48

	within an organism such as chemical levels in tissues or fluids or from evidence of other biomarkers of exposure.	
recovery	The rate and extent of return of a population or community to some aspect(s) of its previous condition. Because of the dynamic nature of ecological systems, the attributes of a "recovered" system should be carefully defined.	124
reference dose (RfD)	An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments. [Durations include acute, short-term, subchronic, and chronic and are defined individually in this glossary] [1] An estimate of the daily exposure dose that is likely to be without deleterious effect even if continued exposure occurs over a lifetime. Related term: Acceptable Daily Intake [26]	55, 125, 187
reference dose (RfDDT) or reference concentration (RfCDT) for development toxicity	REFERENCE DOSE (RfDDT) OR REFERENCE CONCENTRATION (RfCDT) FOR DEVELOPMENTAL TOXICITY. The RfDDT or RfCDT is an estimate of a daily exposure to the human population that is assumed to be without appreciable risk of deleterious developmental effects. The use of the subscript DT is intended to distinguish these terms from the reference dose (RfD) for oral or dermal exposure or the reference concentration (RfC) for inhalation exposure, terms that refer primarily to chronic exposure situations (U.S. EPA, 1991b). The RfDDT or RfCDT is derived by applying uncertainty factors to the NOAEL (or the LOAEL, if a NOAEL is not available), or the benchmark dose. To date, the Agency has applied uncertainty factors only to the NOAEL or LOAEL to derive an RfDDT or RfCDT. The Agency is planning eventually to use the benchmark dose approach as the basis for derivation of the RfDDT or RfCDT and will develop guidance as information is acquired and analyzed from ongoing Agency studies. The most sensitive developmental effect (i.e., the critical effect) from the most appropriate and/or sensitive mammalian species is used for determining the NOAEL, LOAEL, or the benchmark dose in deriving the RfDDT or RfCDT (Section 3.2). Uncertainty factors (UFs) for developmental and maternal toxicity applied to the NOAEL generally include a 10-fold factor for interspecies variation and a 10-fold factor for intraspecies variation. In general, an uncertainty factor is not applied to account for duration of exposure. Additional factors may be applied to account for other uncertainties or additional information that may exist in the database. In circumstances	127

	where only a LOAEL is available, the use of an additional uncertainty factor of up to 10 may be required, depending on the sensitivity of the endpoints evaluated, adequacy of dose levels tested, or general confidence in the LOAEL.	
reference level of risk	Descriptions of a "reference level of risk" in relation to water are typically expressed in terms of specific health outcomes – for example, a maximum frequency of diarrhoeal disease or cancer incidence or maximum frequency of infection (but not necessarily disease) with a specific pathogen.	176
reference value (RfV)	An estimate of an exposure for a given duration to the human population (including susceptible subgroups) that is likely to be without an appreciable risk of adverse health effects over a lifetime. It is derived from a BMDL, a NOAEL, a LOAEL, or another suitable point of departure, with uncertainty/variability factors applied to reflect limitations of the data used. [Durations include acute, short-term, subchronic, and chronic and are defined individually in this glossary.] [Reference value is a term proposed in the report, "A Review of the Reference Dose and Reference Concentration Processes" (EPA, 2002), and is a generic term not specific to a given route of exposure. EPA develops numerical toxicity values for the RfD and RfC only; no numerical toxicity values are developed for the RfV.	125
regional deposited dose (ROD)	The deposited dose of particles calculated for the region of interest as related to the observed effect. For respiratory effects of particles, the deposited dose is adjusted for ventilatory volumes and the surface area of the respiratory region effected (mg/min-sq.cm). For extra respiratory effects of particles, the deposited dose in the total respiratory system is adjusted for ventilatory volumes and body weight (mg/min-kg) [8] The deposited dose of particles calculated for a respiratory tract region of interest (r) as related to an observed toxicity. For respiratory effects of particles, the deposited dose is adjusted for ventilatory volumes and the surface area of the respiratory region effected (mg/min-sq. cm). For extra respiratory effects of particles, the deposited dose in the total respiratory system is adjusted for ventilatory volumes and body weight (mg/min-kg).[1]	77, 125
regional deposited dose ratio (RDDR) –	The ratio of the regional deposited dose calculated for a given exposure in the animal species of interest to the regional deposited dose of the same exposure in a human. This ratio is used to adjust the exposure effect level for interspecies dosimetric differences to derive a human equivalent concentration for particles.	125
regional gas dose (RGD)	The gas dose calculated for the region of interest as related to the observed effect for respiratory effects. The deposited dose is adjusted for ventilatory volumes and the surface area of the	125

	respiratory region effected (mg/min-sq.cm).	
regional gas dose ratio (RGDR)	The ratio of the regional gas dose calculated for a given exposure in the animal species of interest to the regional gas dose of the same exposure in humans. This ratio is used to adjust the exposure effect level for interspecies dosimetric differences to derive a human equivalent concentration for gases with respiratory effects.	125
relative potency	A comparison of the potency of two or more reference chemicals. Potency of a test chemical is reviewed at all levels of biological organization (subcellular, cellular, animal, human).	77
relative potency factor (RPF)	The ratio of the toxic potency of a given chemical to that of an index chemical in the CAG. Relative potency factors are used to convert exposures of all chemicals in the CAG into their exposure equivalents of the index chemical. Relative Potency Factor (RPF) Method: The RPF approach expresses the potency of each chemical in a CAG in relation to the potency of another member in the group which has been selected as the index chemical. A relative potency factor is calculated for each chemical for each route of exposure (e.g., oral, dermal, inhalation). For example, if compound A is determined to be one-tenth as toxic as the index compound the RPF for compound A is 0.1. Using this approach, for each route of exposure for each chemical, exposure is expressed as exposure equivalents of the index chemical. The exposure equivalents are calculated by multiplying the residues and the RPF for each route. These exposure equivalents are summed to obtain an estimate of total exposure by route in terms of the index chemical.	149, 176
relative risk (or Risk Ratio (RR))	The relative measure of the difference in risk between the exposed and unexposed populations in a cohort study. The relative risk is defined as the rate of disease among the exposed divided by the rate of the disease among the unexposed. A relative risk of 2 means that the exposed group has twice the disease risk as the unexposed group [1]. The ratio of the rate of the disease (usually incidence or mortality) among those exposed to the rate among those not exposed.[8]. relative risk (RR) is the risk of an event (or of developing a disease) relative to exposure. Relative risk is a ratio of the probability of the event occurring in the exposed group versus the control (non-exposed) group. $RR = \frac{p_{\text{exposed}}}{p_{\text{control}}}$ For example, if the probability of developing lung cancer among smokers was 20% and among non-smokers 10%, then the relative risk of cancer associated with smoking would be 2. Smokers would be twice as likely as non-smokers to develop lung cancer	77, 125

	In a simple comparison between an experimental group and a control group: A relative risk of 1 means there is no difference in risk between the two groups. A RR of < 1 means the event is less likely to occur in the experimental group than in the control group. A RR of > 1 means the event is more likely to occur in the experimental group than in the control group. Relative Risk Definition: Relative risk is a measure of how much a particular risk factor (say cigarette smoking) influences the risk of a specified outcome (say, death by age 70). For example, a relative risk of 2 associated with a risk factor means that persons with that risk factor have a 2 fold increased risk of having a specified outcome compared to persons without that risk factor. A relative risk of 0.5 means that persons with that risk factor have half the risk of the specified outcome (a protective effect) compared to persons without the risk (protective) factor. The Two by Two Table Outcome + - ----------------------- | | | + | A | B | C | | | Factor |----------------------- | | | - | D | F | G | | | ----------------------- | | | | H | I | J Basically there are two types of studies that quantitate risk: Cohort study: groups with different exposures (potential risk or protective factors) are followed over time and selected health outcomes are noted. Case Control Study: groups of sick people (with selected health outcomes) are compared to well persons to see if risk (or protective) factors can be identified that might account for the ill-health. Which of the two types of studies do	

	you think is the less expensive? Now here's a neat trick the statisticians worked out. In case control studies the odds ratio - calculated by A*F/B*D is about equal to the relative risk. The relative risk is a statistic measured in cohort studies - calculated by (A/C)/(D/G).	
relative risk assessment	a process that involves estimating the risks associated with stressors or management actions that often uses qualitative risk techniques. A process similar to comparative risk assessment. It involves estimating the risks associated with different stressors or management actions. To some, relative risk connotes the use of quantitative risk techniques, while comparative risk approaches more often rely on professional judgment. Others do not make this distinction.	124
release rate	The quantity of a pollutant released from a source over a specified period of time.	77
relevance	covering the extent to which data and tests are appropriate for a particular hazard identification or risk characterisation	158
reliability	The probability a system performs a specified function or mission under given conditions for a prescribed time	77
reportable quantity	Quantity of a hazardous substance that triggers reports under CERCLA. If a substance exceeds its RQ, the release must be reported to the National Response Center, the State Emergency Response Commission, and community emergency coordinators for areas likely to be affected.	77
reproducibility	The degree of variation obtained when the same measurement is made with similar instruments and many operators.	77
reproductive toxicity	Influence on reproductive function and posterity. Reproductive toxicity - The occurrence of biologically adverse effects on the reproductive systems of females or males that may result from exposure to environmental agents. The toxicity may be expressed as alterations to the female or male reproductive organs, the related endocrine system, or pregnancy outcomes. The manifestation of such toxicity may include, but not be limited to, adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behavior, fertility, gestation, parturition, lactation, developmental toxicity, premature reproductive senescence, or modifications in other functions that are dependent on the integrity of the reproductive systems. Add: adverse effect on sexual function and fertility"	123
reserve volume	The volume of air remaining in the lungs after a maximal expiration.	125

residence time	The period of time during which a substance resides in a designated area.	77
residual volume (RV)	The lung volume after maximal expiration (TLC – VC).	125
respirable particles	Particle of the size (<5.0 µm) most likely to be deposited in the pulmonary portion of the respiratory tract.	77
response	The proportion or absolute size of a population that demonstrates a specific effect. May also refer to the nature of the effect [8]. Change developed in the state or dynamics of an organism, system or (sub) population in reaction to exposure to an agent [26]. change developed in the state or dynamics of a system in reaction to the action of an agent[11]	21, 52, 55, 77
response additivity	When the toxic response (rate, incidence, risk, or probability of effects) from the combination is equal to the conditional sum of component responses as defined by the formula for the sum of independent event probabilities. For two chemical mixtures, the body's response to the first chemical is the same whether or not the second chemical is present.	131
retrospective risk assessment	An evaluation of the causal linkages between observed ecological effects and stressor(s) in the environment.	124
risk	The potential for realization of unwanted, adverse consequences to human life, health, property, or the environment; estimation of risk is usually based on the expected value of the conditional probability of the event occurring times the consequence of the event given that it has occurred [8]. The probability of adverse effects caused under specified circumstances by an agent in an organism, a population, or an ecological system [11]. Risk is the likelihood that a loss of sustainable ecological function will occur. This definition emphasises two important aspects: • An a priori decision as to what the undesired event is (i.e. loss of sustainable ecological function) • A realisation that there is uncertainty about the event which is expressed in terms of a likelihood. It may not be possible to assess the likelihood of this event directly ('statutory risk') and it may be that the risk of surrogate events may have to be assessed ('surrogate risk') in order to assess the statutory risk. Webster: possibility of loss or injury : 2 : someone or something that creates or suggests a hazard 3 a : the chance of loss or the perils to the subject matter of an insurance contract; also : the degree of probability of such loss b : a person or thing that is a specified hazard to an insurer <a poor risk for insurance> c : an insurance hazard from a specified cause or source <war risk> 4 : the chance that an investment (as a stock or commodity) will lose value	21, 77, 91

risk (in the context of human health)	The probability of adverse effects resulting from exposure to an environmental agent or mixture of agents [1]. The probability of injury, disease, or death under specific circumstances. In quantitative terms, risk is expressed in values ranging from zero (representing the certainty that harm will not occur) to one (representing the certainty that harm will occur). [14]. The probability of an adverse effect in an organism, system or (sub) population caused under specified circumstances by exposure to an agent [26].	21, 27, 55, 125, 187
risk analysis	A detailed examination including risk assessment, risk evaluation, and risk management alternatives, performed to understand the nature of unwanted, negative consequences to human life, health, property, or the environment; an analytical process to provide information regarding undesirable events; the process of quantification of the probabilities and expected consequences for identified risks[8]. A process for controlling situations where an organism, system or (sub) population could be exposed to a hazard. The Risk Analysis process consists of three components: risk assessment, risk management and risk communication [26]. Process for controlling situations where populations or ecological systems could be exposed to a hazard. It usually comprises three steps, namely risk assessment, risk management, and risk communication.[11]. A process for controlling situations where an organism, system or (sub) population could be exposed to a hazard. The Risk Analysis process consists of three components: risk assessment, risk management and risk communication [61.	21, 52, 55, 77, 69
risk assessment	The process of establishing information regarding acceptable levels of a risk and/or levels of risk for an individual, group, society, or the environment [8]. Risk Assessment (in the context of human health): The evaluation of scientific information on the hazardous properties of environmental agents (hazard characterization), the dose-response relationship (dose-response assessment), and the extent of human exposure to those agents (exposure assessment). The product of the risk assessment is a statement regarding the probability that populations or individuals so exposed will be harmed and to what degree (risk characterization) [1]. The determination of the kind and degree of hazard posed by a chemical, the extent to which a particular group of people has been or may be exposed to the chemical, and the present or potential health risk that exists due to the chemical.[12]. A process intended to calculate or estimate the risk to a given target organism, system Or (sub)population , including the identification of attendant uncertainties, following exposure to a particular agent, taking into account the inherent characteristics of the agent of concern as	21, 27, 52, 55, 125

	well as the characteristics of the specific target system. The Risk Assessment process includes four steps: hazard identification, hazard characterisation (related term: dose-response assessment), exposure assessment, and risk characterization. It is the first component in a risk analysis process [26]. Process intended to calculate or estimate the risk for a given target system following exposure to a particular substance, taking into account the inherent characteristics of a substance of concern as well as the characteristics of the specific target system. The process includes four steps: hazard identification, dose-response assessment, exposure assessment, and risk characterization. It is also the first step in risk analysis [11].	
risk characterization	The integration of information on hazard, exposure, and dose-response to provide an estimate of the likelihood that any of the identified adverse effects will occur in exposed people[1]. The qualitative and, wherever possible, quantitative determination, including attendant uncertainties, of the probability of occurrence of known and potential adverse effects of an agent in a given organism, system or (sub)population, under defined exposure conditions. Risk Characterisation is the fourth step in the Risk Assessment process [26]. Integration of evidence, reasoning, and conclusions collected in hazard identification, dose-response assessment, and exposure assessment and the estimation of the probability, including attendant uncertainties, of occurrence of an adverse effect if an agent is administered, taken, or absorbed by a particular organism or population. It is the last step of risk assessment. Note: In ecological risk assessment, concentration-response assessment is carried out instead of dose-response assessment. or qualitative and/or quantitative estimation, including attendant uncertainties, of the severity and probability of occurrence of known and potential adverse effects of a substance in a given population [11] A phase of ecological risk assessment that integrates the exposure and stressor response profiles to evaluate the likelihood of adverse ecological effects associated with exposure to a stressor. Lines of evidence and the adversity of effects are discussed [40].	21, 52, 55, 69, 124, 125
risk comminication	Interactive exchange of information about (health or environmental) risks among risk assessors, managers, news media, interested groups and the general public [26].	52, 55, 69
risk estimation	The scientific determination of the characteristics of risks, usually in as quantitative a way as possible. These include the magnitude, spatial scale, duration and intensity of adverse consequences and their associated probabilities as well as a description of the cause and effect links [8].	21, 52, 55, 69, 77

	Quantification of the probability, including attendant uncertainties, that specific adverse effects will occur in an organism, system or (sub)population due to actual or predicted exposure [26]. Quantification of the probability, including attendant uncertainties, that a chemical, physical, or biological agent administered, taken, or absorbed by a system with have a specific effect, based on hazard identification, dose-response assessment, and exposure assessment for that particular agent in relation to that particular system [11 The quantification of dose-effect and dose-response relationships for a given environmental agent, showing the probability and nature of health effects of exposure to the agent (WHO, 1988). Assessment, with or without mathematical modelling, of the probability and nature of effects of exposure to a substance based on quantification of dose-effect and dose-response relationships for that substance and the population(s) and environment components likely to be exposed and on assessment of the levels of potential exposure of people, organisms and environment at risk [OECD, 1996].	
risk evaluation	A component of risk assessment in which judgments are made about the significance and acceptability of risk [8]. Risk Evaluation Establishment of a qualitative or quantitative relationship between risks and benefits of exposure to an agent, involving the complex process of determining the significance of the identified hazards and estimated risks to the system concerned or affected by the exposure, as well as the significance of the benefits brought about by the agent. It is an element of risk management. Risk Evaluation is synonymous with Risk-Benefit evaluation [26]. risk evaluation: establishment of a qualitative or quantitative relationship between risks and benefits, involving the complex process of determining the significance of the identified hazards and estimated risks to those organisms or people concerned with or affected by them. It is the first step in risk management. Note: It is synonymous with risk-benefit evaluation [11]. In the Context of the Rotterdam Convention "The term 'risk evaluation' used in Annex I and Annex II is understood by the Intergovernmental Negotiating Committee to be not a risk assessment, but rather an evaluation of intrinsic toxicological and ecotoxicological properties and actual or expected relevant exposure, including actual incidents and scientific evidence of hazard." Risk evaluation is neither hazard assessment nor risk assessment, but something in between. Risk evaluation considers information on hazard and exposure. In notifications of final regulatory actions to ban or severely restrict a chemical: (a) Information on hazard assessment is normally based on	21, 52, 55, 69, 77

	internationally accepted toxicological or ecotoxicological data; (b) Information on exposure is to be related to the prevailing conditions of use in the notifying country. Information to be contained in the supporting documentation provided by a notifying country using a risk evaluation from another country in support of final regulatory action.	
risk factors	A risk factor is an attribute or exposure which is causally associated with an increased probability of a disease or injury.	27
risk identification	Recognizing that a hazard exists and trying to define its characteristics. Often risks exist and are even measured for some time before their adverse consequences are recognized. In other cases, risk identification is a deliberate procedure to review, and it is hoped, anticipate possible hazards.	77
risk management(in the context of human health)	A decision making process that accounts for political, social, economic and engineering implications together with risk-related information in order to develop, analyze and compare management options and select the appropriate managerial response to a potential chronic health hazard [1]. Decision-making process involving considerations of political, social, economic, and technical factors with relevant risk assessment information relating to a hazard so as to develop, analyse, and compare regulatory and non-regulatory options and to select and implement appropriate regulatory response to that hazard. Risk management comprises three elements: risk evaluation; emission and exposure control; risk monitoring [26]. Decision-making process involving considerations of political, social, economic, and technical factors with relevant risk assessment information relating to a hazard so as to develop, analyze, and compare regulatory and nonregulatory options and to select and implement the optimal decisions and actions for safety from that hazard. Essentially, risk management is the combination of three steps: risk evaluation, emission and exposure control, and risk monitoring.	21, 52, 55, 69, 125
risk monitoring	Process of following up the decisions and actions within risk management in order to ascertain that risk containment or reduction with respect to a particular hazard is assured. Risk monitoring is an element of risk management [26]. process of following up the decisions and actions within risk management in order to ascertain that risk containment or reduction with respect to a particular hazard is assured [11]. The process of following up decisions and actions within risk management in order to check whether the aims of reduced exposure and risk are achieved (WHO, 1988) [OECD, 1996].	21, 52, 55, 69
risk pooling	The practice of bringing several risks together for insurance purposes in order to balance the consequences of the realization	183

	of each individual risk [6]	
risk rating	Technique for adjusting insurance premiums according to the relative risk insured [6]	183
risk selection	The practice of singling out or disaggregating a particular risk from a pool of insured risks.	183
risk-specific dose (RSD) , risk - specific concentration (RSC)	Risk Specific Concentration. The risk value of a chemical in mg/cu.m that is associated with a specified excess lifetime cancer risk, usually an upper 95% confidence limit. In ITER, all RSCs are calculated by TERA from the organization's unit risk or TC05 and represent the risk at a 1 in 100,000 (E-5) level. Risk Specific Dose. The risk value of a chemical in mg/kg-day that is associated with a specified excess lifetime cancer risk, usually an upper 95% confidence limit. In ITER, the RSDs for the U.S. EPA and Health Canada are calculated by TERA from the organization's slope factor or TD05, respectively, and represent the 1 in 100,000 (E-5) risk level. NSF International calculates a human equivalent dose at the 10-5 risk level that is then used to calculate the TAC in drinking water.	12
risk value	A dose in mg of chemical per kg of body weight per day (expressed as mg/kg-day), or concentration of chemical in mg of chemical per cubic meter of air (expressed as mg/cu.m) that for noncancer toxicity is generally considered to be without adverse effects in populations of humans (including sensitive subpopulations) for the duration of exposure specified. Examples of noncancer risk values include: MRL, RfD, RfC, TC, TDI. For cancer toxicity, this dose or concentration is usually associated with a specified lifetime cancer risk from exposure to the chemical. Examples of cancer risk values include: CR(inhal), CR(oral), RSC, RSD, TD05, TC05. NOTE: A "p" listed before a risk value indicates that it is a provisional value.	12
route of exposure	The way in which a person may contact a chemical substance. For example, drinking (ingestion) and bathing (skin contact) are two different routes of exposure to contaminants that may be found in water. See "Exposure".	66, 118, 149
safety	Relative protection from adverse consequences [8]. Practical certainty that adverse effects will not result from exposure to an agent under defined circumstances. It is the reciprocal of risk.[26]. Practical certainty that adverse effects will not be caused by an agent under defined circumstances.Note: It is a reciprocal of risk [11]. Strictly, free from harm or risk. Exposure to a chemical usually has some risk associated with it, although the risk may be very small. However, many people use the word safe to mean something that has a very low risk or one that is acceptable to them [29]	21, 55, 66, 69, 77, 91, 187

safety factor	Composite (reductive) factor by which an observed or estimated no-observed-adverse effect level (NOAEL) is divided to arrive at a criterion or standard that is considered safe or without appreciable risk. Related terms: Assessment Factor, Uncertainty Factor[26]. Factor by which an observed or estimated toxic concentration or dose is divided to arrive at a criterion or standard that is considered safe [11]	21, 55, 69, 187
secondary effect	An effect where the stressor acts on supporting components of the ecosystem, which in turn have an effect on the ecological component of interest (synonymous with indirect effects; compare with definition for primary effect).	124
sensitivity analysis	Systematic investigation of the effects on estimates or outcomes of changes in data or parameter inputs or assumptions [12]. Refers to the variation in output of a model with respect to changes in the values of the model input(s). Sensitivity analysis can provide a quantitative ranking of the model inputs based on their relative contributions to model output variability and uncertainty	27
severity	This is the degree to which an effect changes and impairs the functional capacity of an organ system.	27, 47
short-term exposure	Repeated exposure by the oral, dermal, or inhalation route for more than 24 hours, up to 30 days.	125
short-term reference concentration (RfC)	An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for short-term duration (up to 30 days) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.	125
short-term reference dose (RfD)	An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure for a short-term duration (up to 30 days) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.	125
SIDS (Screening Information Data Set)	Screening Information Data Set: The data set of the OECD Existing Chemicals Programme comprises data on chemical identity, physical-chemical data, exposure information, environmental fate and pathways, ecotoxicological data and toxicological data.	31

sink	A place where pollutants are collected by means of processes such as absorption. The opposite of source.	77
slope factor (SF, CPSF)	An upper bound, approximating a 95% confidence limit, on the increased cancer risk from a lifetime exposure to an agent. This estimate, usually expressed in units of proportion (of a population) affected per mg/kg-day, is generally reserved for use in the low-dose region of the dose-response relationship, that is, for exposures corresponding to risks less than 1 in 100.	125
smoke	The visible aerosol that results from incomplete combustion	77
soil adherence	The property of a material which causes it to be retained on the surface of the epidermis (adheres to the skin).	48
source	A place where pollutants are emitted, for example a chimney stack.	50, 77
source-to-dose model	An approach where an environmental agent is followed from its source to the resulting dose [44]. The origin of an agent released into the environment [49].	50
SPEGL (Short-term Public Exposure Guidance Levels)	The Short-term Public Exposure Guidance Levels (SPEGL) were developed by the NRC COT as public exposure guidelines, mostly for civilian populations around military bases (which are similar to civilian populations anywhere else). Effects were considered for all groups of the public. Only five SPEGLs have been developed: hydrazine, dimethylhydrazine, monomethyl hydrazine, nitrogen dioxide, and hydrogen chloride. While applicable to spill response situations, the short list of SPEGLs covers only a small fraction of the large number of chemicals that may spill and pose a risk to the publicThe Short-term Public Emergency Guidance Level (SPEGL) is defined by the National Academy of Sciences (NRC, 1986) as a suitable concentration for unpredicted, single, short-term, emergency exposure of the general public. In contrast to the EEGL, the SPEGL takes into account the wide range of susceptibility of the general public, but it is not designed for repeated or multiple exposures.	9
stakeholder	a person, group of people, an organization (public or private), a business, or other party that has an interest in terms of knowledge or jurisdiction or is affected in terms of their health, property rights, or economy by an environmental risk (s) [2]. Any party to a transaction which has particular interests in its outcome[6].	137, 183
standardized mortality ratio (SMR)	The ratio of observed deaths in a population to the expected number of deaths as derived from rates in a standard population with adjustment of age and possibly other factors such as sex or race [8]. This is the relative measure of the difference in risk between the exposed and unexposed populations in a cohort study. The SMR is similar to the relative risk in both definition and interpretation.	77, 125

	This measure is usually standardized to control for any differences in age, sex, and/or race between the exposed and reference populations. It is frequently converted to a percent by multiplying the ratio by 100 [1]	
stationary sources	A pollution location that is fixed rather than moving.	77
statistical significance	The statistical significance determined by using appropriate standard techniques of statistical analysis with results interpreted at the stated confidence level and based on data relating species which are present in sufficient numbers at control areas to permit a valid statistical comparison with the areas being tested [8].The probability that a result is not likely to be due to chance alone. By convention, a difference between two groups is usually considered statistically significant if chance could explain it only 5% of the time or less. Study design considerations may influence the a priori choice of a different level of statistical significance [1]	77, 125
statistically significant effect	In statistical analysis of data, a health effect that exhibits differences between a study population and a control group that are unlikely to have arisen by chance alone.	48
steady state exposure	Exposure to an environmental pollutant whose concentration remains constant for a period of time.	48, 77
STEL	The Short-Term Exposure Level (STEL) is the maximum concentration of a contaminant (generally in mg/L) that is permitted in drinking water for an acute exposure period, calculated and applied in accordance with Annex A of NSF/ANSI 61. The drinking water concentration is required to decay to a level at or below the TAC or SPAC within 90 days. Used by NSF International[14]. the maximum permissible concentration of a material, generally expressed in ppm in air, for a defined short period of time (typically 5 minutes). These values, which may differ from country to country, are often backed up by regulation and therefore may be legally enforceable.	12
stochastic model	A mathematical model which takes into consideration the presence of some randomness in one or more of its parameters or variables. The predictions of the model therefore do not give a single point estimate but a probability distribution of possible estimates. Contrast with deterministic.	48
stress regime	The term “stress regime” has been used in at least three distinct ways: (1) to characterize exposure to multiple chemicals or to both chemical and nonchemical stressors (more clearly described as multiple exposure, complex exposure, or exposure to mixtures), (2) as a synonym for exposure that is intended to avoid overemphasis on chemical exposures, and (3) to describe the series of interactions of exposures and effects resulting in secondary exposures, secondary effects and, finally, ultimate effects (also known as risk cascade	124

stressor	Any physical, chemical, or biological entity that can induce an adverse response (synonymous with agent) [40]. Any entity, stimulus, or condition that can modulate normal functions of the organism or induce an adverse response (e.g., agent, lack of food, drought) [49].	124
stressor-response profile	The product of characterization of ecological effects in the analysis phase of ecological risk assessment. The stressor-response profile summarizes the data on the effects of a stressor and the relationship of the data to the assessment endpoint.	124
subchronic exposure	Repeated exposure by the oral, dermal, or inhalation route for more than 30 days, up to approximately 10% of the life span in humans (more than 30 days up to approximately 90 days in typically used laboratory animal species). [See also longer-term exposure.][1]. A contact between an agent and a target of intermediate duration between acute and chronic [49] .	50, 125
subchronic reference concentration (RfC)	An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for a subchronic duration (up to 10% of average lifespan) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.	125
subchronic reference dose (RfDs)	An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure for a subchronic duration (up to 10% of average lifespan) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.	125
subchronic study	A toxicity study designed to measure effects from subchronic exposure to a chemical.	125
subjective environment (synonym: perceived environment)	The environment as it is perceived by persons living in it, e.g. eye irritation caused by air pollution, or pleasure arising from good housing conditions (WHO, 1979). Surrounding conditions as perceived by persons living in these conditions [OECD, 1996].	
sufficient evidence	A term used in evaluating study data for the classification of a carcinogen under the 1986 U.S. EPA guidelines for carcinogen risk assessment. This classification indicates that there is a causal relationship between the agent or agents and human cancer[1].The IARC Working Group considers that a causal	125

	relationship has been established between exposure to the agent and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence. A statement that there is sufficient evidence is followed by a separate sentence that identifies the target organ(s) or tissue(s) where an increased risk of cancer was observed in humans. Identification of a specific target organ or tissue does not preclude the possibility that the agent may cause cancer at other sites.	
Superfund	Federal authority, established by the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) in 1980, to respond directly to releases or threatened releases of hazardous substances that may endanger health or welfare [8]. The federal and state programs to investigate and clean up inactive hazardous waste sites [29]	66, 77
supporting studies	Studies that contain information useful for providing insight and support for conclusions.	125
surrogate	Something that serves as a substitute. In risk analysis, surrogates are often used when data on the item of interest (a chemical, an industry, an exposure, etc.) is lacking. As an example, underground mining of coal and hardrock minerals can be used as a surrogate for underground oil shale mining.	77
surrogate dose	A surrogate dose is specific to a combination of facility, chemical release, media, release pathway and exposure pathway. It is calculated in several steps. First, exposure and release pathway-specific chemical release volumes are combined with physicochemical properties and site-specific characteristics in models to estimate an ambient concentration in the environmental medium of concern. The ambient media concentration is then combined with standard human exposure assumptions (for adults and children) to estimate the magnitude of the dose.	151
susceptibility	Increased likelihood of an adverse effect, often discussed in terms of relationship to a factor that can be used to describe a human subpopulation (e.g., life stage, demographic feature, or genetic characteristic) [1]. Increased likelihood of an adverse effect or an exposure, often discussed in terms of relationship to a factor that can be used to describe a human subpopulation (e.g., life stage, demographic feature, or genetic characteristic).	125
susceptible populations (susceptible subgroups)	May refer to life stages, for example, children or the elderly, or to other segments of the population, for example, asthmatics or the immune-compromised, but are likely to be somewhat chemical-specific and may not be consistently defined in all cases [1]. May refer to life stages, e.g., children or the elderly, or to other segments of the population, e.g., asthmatics, the immune-	125

	compromised, or the highly exposed. The term is likely to be somewhat chemical-specific, and may not be consistently defined in all cases [44].	
synergetic	Working together; an agent that works synergistically with one or more other agents.	77
synergism	An interaction between two substances that results in a greater effect than both of the substances could have had acting independently[8]. When a reaction between the chemicals has occurred and a different chemical is formed. The toxic effect produced is greater than that suggested by the component toxic effects, and may be different from effects produced by either chemical by itself. When the effect of the combination is greater than that suggested by the component toxic effects. Synergism must be defined in the context of the definition of "no interaction," which is usually dose or response addition [109].	77, 131
synergistic interaction	Joint effects of two or more agents, such as drugs that increase each other's effectiveness when taken together [8]. A synergistic effect is the any effect of two chemicals acting together which is greater than the simple sum of their effects when acting alone: such chemicals are said to show synergism [55]..	48, 77, 131
synopsis	brief description of the available risk values describing differences when appropriate [14].	12
systematic error	A reproducible inaccuracy introduced by faulty equipment, calibration, or technique.	48, 77
systemic effects (or systemic toxicity)	Toxic effects as a result of absorption and distribution of a toxicant to a site distant from its entry point.[1]. Systemic effects are those that require absorption and distribution of the toxicant to a site distant from its entry point, at which point effects are produced. Most chemicals that produce systemic toxicity do not cause a similar degree of toxicity in all organs, but usually demonstrate major toxicity to one or two organs. These are referred to as the target organs of toxicity for that chemical. [14]	12, 125
target	A physical, biological, or ecological object. Examples of targets are humans, human organs and animals [49].	50
target organ/system	The biological organ(s) most adversely affected by exposure to a chemical, physical, or biological agent[1]. The organ or system of the body that is generally affected first as the dose of the chemical is increased from zero. For noncancer toxicity, the critical effect occurs in the primary target organ. Often, multiple organs or systems are impacted by a chemical at its lowest effective dose or concentration [14]	12, 125
target population	1. The collection of individuals, items, measurements, etc., about	48

	which we want to make inferences. The term is sometimes used to indicate the population from which a sample is drawn and sometimes which inferences are required. 2. The group of persons for whom an intervention is planned.	
TC05 - tumourigenic concentration (05)	is the concentration in air (expressed in mg/cu.m) associated with a 5% increase in incidence or mortality due to tumours. The TC05 is not based on the confidence limit but rather, is computed directly from the curve. Health Canada calculates TC05s for compounds classified in Groups I and II basing these values on tumours observed in epidemiological studies (generally) in occupationally exposed human populations, or those considered relevant to humans as observed in bioassays in experimental animals. The estimates of potency are generally restricted to effects for which there has been a statistically significant increase in incidence and a dose-response relationship, characterized by appropriate mathematical models (e.g. multistage). The Health Canada TC05 can be divided by a suitable margin, to provide a benchmark against which the adequacy of intake can be judged, with respect to potential carcinogenicity.	12
temperature inversion	Layer of air in which temperature increases with altitude; very little turbulent exchange occurs within it. Layer of air in which temperature increases with altitude; very little turbulent exchange occurs within it.	77
TERA	Toxicology Excellence for Risk Assessment (TERA) is a nonprofit research and education organization dedicated to the best use of toxicity data for risk values. TERA staff can be reached by phone: U.S. 513-542-RISK (7475); Fax: U.S. 513-542-7487; or email: tera@tera.org.	12
teratogenic	Substances that are suspected of causing malformations or serious deviations from the normal type, which can not be inherited in or on animal embryos or fetuses [8]. Structural developmental defects due to exposure to a chemical agent during formation of individual organs [1]. Malformations and variations - A malformation is usually defined as a permanent structural change that may adversely affect survival, development, or function. The term teratogenicity is used in these Guidelines to refer only to malformations. The term variation is used to indicate a divergence beyond the usual range of structural constitution that may not adversely affect survival or health. Distinguishing between variations and malformations is difficult since there exists a continuum of responses from the normal to the extremely deviant. There is no generally accepted classification of malformations and variations. Other terms that are often used, but no better defined, include anomalies, deformations, and aberrations.	77, 125, 127
teratology	Science that deals with abnormal development of the fetus and	77

	congenital malformation.	
theoretical-minimum-risk exposure distribution	The population distribution of exposure to a risk factor that would result in the lowest population disease burden.	27
threshold	A pollutant concentration [or dose] below which no deleterious effect occurs [8]. The dose or exposure below which no deleterious effect is expected to occur [1]. The dose or exposure below which an adverse effect is not expected. Common approaches to assessing the risks associated with noncancer toxicity are generally different from that used to assess the potential risks associated with carcinogenesis. Scientists often assume that a small number of molecular events can evoke carcinogenic and/or mutagenic changes in a single cell, which can lead to self-replicating damage. Often, this is considered a non-threshold effect since there is presumably no level of exposure that does not pose a small, but finite, probability of generating a response. It is most often assumed that noncancer effects have a threshold, that is, a dose level below which a response is unlikely, because a compensatory effect or adaptive effect in the cell protects against an adverse effect. This threshold concept is important in many regulatory contexts. The individual threshold hypothesis holds that some exposures can be tolerated by an organism with essentially no chance for expression of a adverse effect. Further, risk management decisions frequently focus on protecting the more sensitive members of a population. In these cases efforts are made to keep exposures below the more sensitive subpopulation threshold, although it is recognized that hypersensitivity and chemical idiosyncrasy may exist at yet lower doses [14]. Dose or exposure concentration of an agent below that a stated effect is not observed or expected to occur [26]. Dose of a substance or exposure concentration below which a stated effect is not observed or expected to occur [11]	21, 27, 52, 55, 77, 125
threshold dose	The minimum application of a given substance required to produce an observable effect.	77
threshold limit value (TLV)	Refers to airborne concentrations of substances and represents conditions under which it is believed that nearly all workers are protected while repeatedly exposed for an 8-hr day, 5 days a week (expressed as parts per million (ppm) for gases and vapors and as milligrams per cubic meter (mg/m3) for fumes, mists, and dusts) [8]. Threshold Limit Value (TLV): Recommended guidelines for occupational exposure to airborne contaminants published by the American Conference of Governmental Industrial Hygienists (ACGIH). TLVs represent the average concentration in mg/m3 for an 8-hour workday and a 40-hour work week to which nearly all	77, 125

	workers may be repeatedly exposed, day after day, without adverse effect [1]	
time averaged exposure	The time-integrated exposure divided by the exposure duration. An example is the daily average exposure of an individual to carbon monoxide [49].	50
tidal volume (VT)	The volume of air inhaled/exhaled during normal breathing.	125
time extrapolation (concentration-time relationship)	"Haber's Law" states that the product of the concentration (C) and time of exposure (T) required to produce a specific physiologic effect is equal to a constant level or severity of response (K), or C x T = K (Rinehart and Hatch, 1964). When the duration of experimental exposure differs from the desired exposure duration for which an acute exposure level is being calculated (in this case 1 hour), a modification of Haber's Law is used to adjust the experimental exposure duration to the desired duration of the acute exposure level: Cn * x T = K, where n is a chemical-specific parameter greater than zero (ten Berge, 1986). When n is equal to 1 (n=1), the toxicity of a chemical is equally dependent on changes in concentration and duration of exposure; when n is less than 1 (n<1), the duration of exposure is a greater determinant of toxicity than the concentration; finally, when n is greater than 1 (n>1), the toxicity of a chemical is determined to a greater extent by exposure concentration than by duration. Ideally, the magnitude of n should be determined for all chemicals by evaluating the concentration versus response relationships for several different exposure durations. However, this information is available for only a limited number of substances. Empirically derived values of the exponent n range from 0.8-3.5 (ten Berge, 1986). The time-concentration-response relationship depends on the time-frame considered and the endpoint measured. There are usually multiple "n" values for a single chemical that are applicable to different response endpoints. For example, the "n" for irritation of ammonia is 4.6, while the "n" for lethality of ammonia is 2. A risk assessment document published by the NAS (NRC, 1987) includes a general statement that Haber's Law does not apply for "some irritants". However, no specific references are cited by NAS in support of this statement. It is likely that the basis of this statement is the observation that for some substances, irritation appears to be solely concentration dependent. However, the modified Haber's Law presented here is able to accommodate any such empirical observations. For example, in those cases for which data exist to allow the determination of a concentration-time relationship for irritants (e.g. chlorine, ammonia), an analysis by OEHHA revealed that both concentration and time of exposure contributed to the overall severity of effect, as described by Cn x T = K. As concentration becomes the more important factor, the value of "n" will increase. Values of "n" greater than 3 suggest a	147

	strong predominance of concentration over time. When a derived value was not available and there were insufficient data from which to determine a value de novo, a default value for “n” was used. The mean value in this range rounds to 2, while the interquartile range (25%–75%), where most of the “n” values are found, is from 1 to 2,2. When extrapolating from an exposure duration that is greater than 1-hour to a 1-hour level, the value of n=2 was used by OEHHA. When extrapolating from an experimental exposure duration of less than 1 hour to a 1-hour level, the value of n=1 was used. Using a value of n=1 is more health-protective than a value of n=2. A value of n=1 results in a relatively rapid decrease in the derived REL when extrapolations are made from shorter to longer exposures.	
time integrated exposure	The integral of instantaneous exposures over the exposure duration. An example is the area under a daily time profile of personal air monitor readings, with units of concentration multiplied by time.	50
time profile	A continuous record of instantaneous values over a time period (e.g., exposure, dose, medium intake rate).	50
time-weighted average (TWA)	This term is used in the specification of Occupational Exposure Limits (OELs) to define the average concentration of a chemical to which it is permissible to expose a worker over a period of time, typically 8 hours. Time weighted average concentration ((TWA) is a regulatory value defining the concentration of a substance to which a person is exposed in ambient air, averaged over a period, usually 8 hours. For a person exposed to 0.1 mg m_3 for 6 hours and 0.2 mg m_3 for 2 hours, the 8 hour TWA is (0.1 x 6 + 0.2 x 2) / 8 which equals 0.125 mg m_3. The average value of a parameter (such as concentration of an agent in air) that varies over time. [REAP, 1995: Residential Exposure Assessment Project]; c. The average time, over a given work period (e.g., 8 hour work day), of a person's exposure to a chemical or an agent. The average is determined by sampling for the contaminant throughout the time period. Represented as TLV_TWA [55].	48
total allowable concentration (TAC)	is the maximum concentration (generally in mg/L) of a non-regulated contaminant permitted in a public drinking water supply as defined by Annex A of NSF/ANSI 61, a consensus standard developed by consortium including NSF International. Used by NSF International.	12
total lung volume (TLV):	The lung volume at maximal inspiration.	125
total maximum daily loads (TMDLs)	A quantitative expression of the amount of a pollutant that can be present in a waterbody without causing an impairment of the applicable water quality standard for any portion of that water. A TMDL must include wasteload allocation(s) for point sources and load allocation(s) for nonpoint sources plus a margin of safety. A	166

	quantitative expression of the amount of a pollutant that can be present in a waterbody without causing an impairment of the applicable water quality standard for any portion of that water. A TMDL must include wasteload allocation(s) for point sources and load allocation(s) for nonpoint sources plus a margin of safety.	
total suspended particulate matter (TSP)	The total concentration of all airborne particles at a particular point in space.	77
toxic endpoint	quantitative expression of a toxic effect occurring at a given level of exposure. For example, acute lethality is a toxic effect, an LD50 value (median lethal dose) is the toxic endpoint that pertains to the effect.	176
toxicity profile	An examination, summary, and interpretation of a hazardous substance to determine levels of exposure and associated health effects. See our toxicity profiles	77
tolerable daily intake (TDI)	The Tolerable Daily Intake (or Tolerable Intake) expressed on a body weight basis (e.g., mg/kg b.w./day) are the total intakes by ingestion, to which it is believed that a person can be exposed daily over a lifetime without deleterious effect. The TDIs (or TIs) are based on non-carcinogenic effects and are usually calculated by applying uncertainty factors to a NOAEL or LOAEL. Absolute values of maximum intakes per day for various age groups can be developed by multiplying the TDI (or TI) by the average body weight of the age group under consideration. It should be noted, however, that exceedence of such a calculated intake by a particular age group for a small proportion of the lifespan does not necessarily imply that exposure constitutes an undue risk to health. Used by Health Canada and RIVM. Analogous to Acceptable Daily Intake. The term Tolerable is used for agents which are not deliberately added such as contaminants in food.	27, 55, 187
tolerable intake (TI)	Estimate of the amount of a substance that can be ingested or absorbed over a specified period of time without appreciable health risk [11] См. tolerable daily intake (TDI) , Tolerable intake (TI) Estimated maximum amount of an agent, expressed on a body mass basis, to which each individual in a (sub) population may be exposed over a specified period without appreciable risk.	21, 55, 187
total human exposure	Accounts for all exposures a person has to a specific contaminant, regardless of environmental medium or route of entry (inhalation, ingestion, and dermal absorption). Sometimes total exposure is used incorrectly to refer to exposure to all pollutants in an environment . Total exposure to more than one pollutant should be stated explicitly as such. In the conduct of risk assessment (hazard identification, dose_response	48

	assessment, exposure assessment, risk characterization) the need to make assumptions or best judgments in the absence of precise scientific data creates [55]	
toxic substance	A chemical or mixture that may present an unreasonable risk of injury to health or the environment [8]. A chemical, physical, or biological agent that may cause an adverse effect or effects to biological systems [1]	77, 125
toxic wastes	Wastes that contain substances in sufficient quantity to impinge harmfully on biological systems.	77
toxicant	A substance that kills or injures an organism through chemical or physical action or by altering the organism's environment; for example, cyanides, phenols, pesticides, or heavy metals; especially used for insect control.	77
toxicity	The degree of danger posed by a substance to animal or plant life [8]. Deleterious or adverse biological effects elicited by a chemical, physical, or biological agent [1]. Inherent property of an agent to cause an adverse biological effect [26]	55, 77, 69, 125, 187
toxicicodinamics	The determination and quantification of the sequence of events at the cellular and molecular levels leading to a toxic response to an environmental agent (sometimes referred to as pharmacodynamics).	125
toxicology	The study of harmful interactions between chemical, physical, or biological agents and biological systems.	125
trace	A very small amount of a material. Usually used in reference to concentrations which are on the order of or less than 1-10 parts per million.	77
trace metals	Metals normally found in trace amounts due to their insolubility or to their relative lack of abundance in the crust of the earth.	77
transfer coefficient	Residue transfer rate to humans during the completion of specific activities (e.g., cm2 per hour), calculated using concurrently collected environmental residue data.	118
TSCA (Toxic Substances Control Act)	The Toxic Substances Control Act (TSCA) of 1976. In theory, this law gave U.S. EPA the power to test, regulate, and screen nearly all chemicals produced or imported into the United States. However, after more than two decades, TSCA's promise is almost entirely unrealized.	79
Tumor	An abnormal, uncontrolled growth of cells. Synonym: neoplasm	125
Tumor Progression	Under the Armitage-Doll multistage theory of cancer development, the transition of a cell line between the stages which lead to cancer.	125
tumourigenic	is the total intake (often expressed in mg/kg b.w./day) associated	12

dose /tumourogenic concentration - TD05/TC05	with a 5% increase in incidence or mortality due to tumours. The TD05 is not based on the confidence limit but rather, is computed directly from the curve. Health Canada calculates TD05s for compounds classified in Groups I and II basing these values on tumours observed in epidemiological studies (generally) in occupationally exposed human populations, or those considered relevant to humans as observed in bioassays in experimental animals. The estimates of potency are generally restricted to effects for which there has been a statistically significant increase in incidence and a dose-response relationship, characterized by appropriate mathematical models (e.g. multistage). The Health Canada TD05 can be divided by a suitable margin, to provide a benchmark against which the adequacy of intake can be judged, with respect to potential carcinogenicity.	
uncertainty	Uncertainty occurs because of a lack of knowledge. It is not the same as variability. For example, a risk assessor may be very certain that different people drink different amounts of water but may be uncertain about how much variability there is in water intakes within the population. Uncertainty can often be reduced by collecting more and better data, whereas variability is an inherent property of the population being evaluated. Variability can be better characterized with more data but it cannot be reduced or eliminated. Efforts to clearly distinguish between variability and uncertainty are important for both risk assessment and risk characterization [1]. Imperfect knowledge concerning the present or future state of an organism, system or (sub) population under consideration [26]. Imperfect knowledge concerning the present or future state of a system under consideration [11]. SPS Agreement:: The lack of accurate or precise knowledge of the input values which is due to measurement error or to the lack of knowledge of the steps required, and the pathways from hazard to risk, when building the model of the scenario being addressed. It includes uncertainty: 1).Of the process (methodology) ; 2).Of the risk assessor (human error); 3).Of the organisms (biological unknowns)	21, 52, 55, 125
uncertainty/variability factor (UFs):	One of several, generally 10-fold, default factors used in operationally deriving the RfD and RfC from experimental data. The factors are intended to account for (1) variation in susceptibility among the members of the human population (i.e., inter-individual or intraspecies variability); (2) uncertainty in extrapolating animal data to humans (i.e., interspecies uncertainty); (3) uncertainty in extrapolating fromdata obtained in a study with less-than-lifetime exposure (i.e., extrapolating from subchronic to chronic exposure); (4) uncertainty in extrapolating from a LOAEL rather than from a NOAEL; and (5) uncertainty associated with extrapolation when the database is incomplete [1].	21, 52, 55, 125

	Factors representing specific areas of uncertainty inherent in the available data. These are frequently multiples of 10, although different organizations utilize lesser factors when the data allow. The usual uncertainty factors account for: interhuman variability, interspecies variability (extrapolation from animals to humans), extrapolation from less-than-chronic to lifetime exposure, use of a LOAEL instead of a NOAEL, and perhaps an additional factor for the adequacy of the available studies. For a further discussion of the use of uncertainty factors the reader is referred to Dourson et al., 1996; Dourson, 1994; and Barnes and Dourson, 1988. All three documents are available online at http://www.tera.org/pubs [14]. Reductive factor by which an observed or estimated no-observed-adverse effect level (NOAEL) is divided to arrive at a criterion or standard that is considered safe or without appreciable risk. Related terms: Assessment Factor, Safety Factor [26].	
uncertainty analysis	Estimation of range or distribution of uncertainty in estimates based on an assessment of the uncertainty or confidence intervals for all data and parameter inputs. Uncertainty intervals should ideally include all sources of uncertainty, including those arising from systematic biases an measurement error. In contrast, generally reported confidence intervals are based solely on the variation observed in sample data [12]. A detailed examination of the systematic and random errors of a measurement or estimate; an analytical process to provide information regarding the uncertainty [8]	27, 77
unit (cancer) risk (UCR)	The upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 µg/L in water, or 1 µg/m3 in air. The interpretation of unit risk would be as follows: if unit risk = 2 x 10-6 per µg/L, 2 excess cancer cases (upper bound estimate) are expected to develop per 1,000,000 people if exposed daily for a lifetime to 1 µg of the chemical in 1 liter of drinking water [1]. EPA defines unit risk on IRIS as the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 ug/L in water, or 1 ug/cu.m in air. Health Canada Inhalation unit risk derived as: URInh = 0.05/TC05; inhalation slope factor derived as: SFInh = 0.05/(TC05 x 16 m3/day/70.7 kg); For non-carcinogens, TDI and TC values taken directly from Health Canada (1996); for carcinogens, oral slope factor derived as: SForal = 0.05/TD05 [67].	27, 29, 125

unreasonable risk	Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), "unreasonable adverse effects" means any unreasonable risk to man or the environment, taking into account the medical, economic, social, and environmental costs and benefits of any pesticide	77
upper bound	A plausible upper limit to the true value of a quantity. This is usually not a true statistical confidence limit.	125
uptake	The process by which an agent crosses an absorption barrier (see dose).	50
validation	Process by which the reliability and relevance of a particular approach, method, process or assessment is established for a defined purpose. Different parties define “Reliability” as establishing the reproducibility of the outcome of the approach, method, process or assessment over time. "Relevance" is defined as establishing the meaningfulness and usefulness of the approach, method, process or assessment for the defined purpose [26]. Process of assessing whether the predictions or conclusions reached in a risk assessment are correct [11]	21, 52, 55, 69
variability	Variability refers to true heterogeneity or diversity. For example, among a population that drinks water from the same source and with the same contaminant concentration, the risks from consuming the water may vary. This may be due to differences in exposure (i.e., different people drinking different amounts of water and having different body weights, different exposure frequencies, and different exposure durations) as well as differences in response (e.g., genetic differences in resistance to a chemical dose). Those inherent differences are referred to as variability. Differences among individuals in a population are referred to as inter-individual variability, differences for one individual over time is referred to as intra-individual variability. 1. The quality of being subject to variation. 2. A quality of variability and lack of uniformity (Vebster)..	125
well-being	The well-being or quality of life of a population is an important concern in economics and political science. There are many components to well-being. A large part is standard of living, the amount of money and access to goods and services that a person has; these numbers are fairly easily measured. Others like freedom, happiness, art, environmental health, and innovation are far harder to measure and could be more important. This has created an inevitable imbalance as programs and policies are created to fit the easily available economic numbers while ignoring the other measures, that are very difficult to plan for or assess. Debate on quality of life is millennia-old, with Aristotle giving it much thought in his Nicomachean Ethics and eventually settling	168

	on the notion of eudaimonia, a Greek term often translated as happiness, as central. The neologism liveability (or livability), from the adjective liv(e)able, is an abstract noun now often applied to the built environment or a town or city, meaning its overall contribution to the quality of life of inhabitants. Understanding quality of life is today particularly important in health care, where monetary measures do not readily apply. Decisions on what research or treatments to invest the most in are closely related to their effect of a patient's quality of life.	
volatile organic compounds (VOCs)	A VOC is one of a group of carbon-containing compounds that evaporate readily at room temperature. Examples of VOCs include trichloroethane; trichloroethylene; and BTEX (benzene, toluene, ethylbenzene, Xylenes). These contaminants typically are generated from metal degreasing, printed circuit board cleaning, gasoline, and wood preserving processes. chemicals with Henry's Law constants greater than 1E-5 and molecular weight less than 200 are marked as VOCs	151
Weibull model	A dose-response model of the form: $P(d) = \gamma + (1-\gamma)(1 - e^{-\beta d^{\alpha}})$ Where: P(d) = the probability of a tumor (or other response) from lifetime, continuous exposure at dose d until age t (when is fatal); α = fitted dose parameter (sometimes called "Weibull" parameter); β = fitted dose parameter; γ = background response rate.	125
weight-of-evidence for carcinogenicity:	A system used by the U.S. EPA for characterizing the extent to which the available data support the hypothesis that an agent causes cancer in humans. Under EPA's 1986 risk assessment guidelines, the WOE was described by categories "A through E", Group A for known human carcinogens through Group E for agents with evidence of noncarcinogenicity. The approach outlined in EPA's guidelines for carcinogen risk assessment (2005) considers all scientific information in determining whether and under what conditions an agent may cause cancer in humans, and provides a narrative approach to characterize carcinogenicity rather than categories. Five standard weight-of-evidence descriptors are used as part of the narrative. The suggested descriptive terms are as follows: 1). Carcinogenic to humans; 2). Likely to be carcinogenic to humans 3).Suggestive evidence of carcinogenic potential; 4). Inadequate information to assess carcinogenic potential; 5(. Not likely to be carcinogenic to humans	125

worst case	A semiquantitative term referring to the maximum possible exposure, dose, or risk, that can conceivably occur, whether or not this exposure, dose, or risk actually occurs or is observed in a specific population. Historically, this term has been loosely defined in an ad hoc way in the literature, so assessors are cautioned to look for contextual definitions when encountering this term. It should refer to a hypothetical situation in which everything that can plausibly happen to maximize exposure, dose, or risk does in fact happen. This worst case may occur (or even be observed) in a given population, but since it is usually a very unlikely set of circumstances, in most cases, a worst-case estimate will be somewhat higher than occurs in a specific population. As in other fields, the worst-case scenario is a useful device when low probability events may result in a catastrophe that must be avoided even at great cost, but in most health risk assessments, a worst-case scenario is essentially a type of bounding estimate. [USEPA, 1992: GL for Exposure Assessment] [REAP, 1995: Residential Exposure Assessment Project]. The term "worst case exposure" has historically meant the maximum possible exposure, or where everything that can plausibly happen to maximize exposure, happens. While in actuality, this worst case exposure may fall on the uppermost point of the population distribution, in most cases, it will be somewhat higher than the individual in the population with the highest exposure. The worst case represents a hypothetical individual and an extreme set of conditions; this will usually not be observed in an actual population. The worst case and the so-called maximum exposed individual are therefore not synonymous, the former describing a statistical possibility that may or may not occur in the population, and the latter ostensibly describing an individual that does, or is thought to, exist in the population.	48
worst-case scenario	a method of conducting an exposure assessment in which the most conservative value of each input parameter is selected. See also reasonable maximum exposure.	48
xenobiotic	Any biote displaced from its normal habitat; a chemical foreign to a biological system.	77
years lived with disability (YLD)	The component of the DALY (q.v.) that measures lost years of healthy life through living in health states of less than full health (q.v.).	27
years of life lost (YLL)	The component of the DALY (q.v.) that measures years of life lost due to premature mortality.	27
zero order analysis	The simplest approach to quantification of a risk with a limited treatment of each risk component (e.g. source terms, transport, health effects, etc.).	77

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